ABSTRACTS OF WORLD MEDICINE

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Pathology

1354. **The Effect of Hydrocortisone Hemisuccinate on Tracheal Smooth Muscle of the Guinea Pig and Cat**
N. M. LEFCOE. *Journal of Allergy* [*J. Allergy*] **27**, 352–358, July, 1956. 5 figs., 9 refs.

Investigations of the effect of hydrocortisone hemisuccinate, a water-soluble steroid, on tracheal smooth muscle, were made at the Harvard School of Public Health, Boston, on 22 guinea-pigs and 3 cats. The trachea was removed immediately after death and cut into 10 rings which were tied together with thread to form a chain, one end of which was immersed in a bath of Ringer's solution (50 ml.) to which the hemisuccinate was added in increasing doses, and the other connected to a recording apparatus.

It was shown that the resting tone of tracheal muscle was relaxed at an increasing rate by the progressive addition of 30 to 100 mg. of the hemisuccinate to the bath. Histamine-induced contractions were also counteracted by similar doses. This finding is in contrast to the negative effect of hydrocortisone free alcohol reported by others. *H. Herxheimer*

1355. **The Significance of the Order of Application in the Effect of Stimuli on the Development of Pathological Processes.** (Значение последовательности действия раздражителей в развитии патологических процеосах (Экспериментальное исследование))
G. I. KOSITSKII. *Архив Патологии* [*Arkh. Patol.*] **18**, 15–21, No. 1, 1956. 19 refs.

Certain pathological processes caused by specific agents or procedures may be modified by the application of other, non-specific, agents, the effect of the latter depending partly on dose, but mainly on the time of their application in relation to that of the specific agent. Thus in rabbits faradization of the sciatic nerve prevents the onset of adrenaline-induced pulmonary oedema if it is applied before, but not after, the administration of adrenaline, and the protective effect of forced artificial respiration is equally dependent on its being started before the adrenaline is given. Similarly the lethal effect of air embolism in rats can often be prevented by faradization of the sciatic nerve if this is started before the injection of air, whereas faradization performed after the introduction of the air has no such action. The tuberculin reaction in guinea-pigs can be considerably modified by the previous subcutaneous injection of turpentine, but turpentine introduced after the administration of tuberculin to sensitive animals is without effect. On the other hand the results of freezing in rats can be modified if some other part of the body is subjected to faradization either before or after the freezing.

These observations may be interpreted as phenomena of " negative induction " in the central nervous system, the application of the non-specific stimulus causing a state of inhibition in the area of the brain subsequently stimulated as a result of the action of the specific agent. In this way the effect of the latter is modified either by inhibiting some of the effect of the stimulation or by re-shunting it along alternative neural pathways. *L. Crome*

1356. **The Effect of Excessive Strain of the Central Nervous System on Haematopoiesis in Mice.** (Влияние перенапряжения центральной нервной системы на кроветворение у мышей)
E. I. ZHAROVA. *Архив Патологии* [*Arkh. Patol.*] **18**, 42–46, No. 1, 1956. 2 figs., 7 refs.

In experiments at the Central Order of Lenin Institute of Haematology and Blood Transfusion, Moscow, neurotic states were produced in mice by the use of excessively powerful stimuli, sudden delays in the reinforcement of conditioned reflexes, and the frequent association of the conditioned stimuli with the application of electric currents. The effect of this treatment on haematopoiesis, as revealed by examination of the blood and bone marrow, was that an initial stage of erythraemia was followed by anaemia with reticulocytosis and moderate leucopenia. *L. Crome*

1357. **Phosphorus Metabolism in the Erythrocytes in Tuberculous Infections, as Revealed by Means of Radioactive Isotopes.** (Исследование интенсивности фосфорного обмена эритроцитов при туберкулезе методом радиоактивных изотопов)
K. K. NORMAN. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 3–6, No. 3, May–June, 1956. 3 figs.

In tuberculous meningitis and in severe forms of pulmonary tuberculosis, particularly during the phases of diffuse infiltration and caseation, phosphorus metabolism in the erythrocyte is reduced in intensity, tending to return to normal as the condition of the patient improves. This is particularly noticeable in cases of pulmonary and meningeal tuberculosis successfully treated with specific chemotherapeutic agents which do not influence the phosphorus metabolism of the erythrocytes when given to healthy animals. *A. Orley*

1358. **The Penetration of Radioactive Phosphorus through Normal and Damaged Skin.** (Проникновение радиоактивного фосфора внутрь организма через нормальную и поврежденную кожу)
N. N. GRANOVSKAYA. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 7–11, No. 3, May–June, 1956. 3 figs., 13 refs.

Disodium phosphate prepared with radioactive phosphorus ($Na_2H^{32}PO_4$) applied to the intact skin of animals in concentrations of 2·5 to 7·5 mc. per sq. cm. of skin either in watery solution or incorporated in a lanolin ointment does not penetrate into the animal organism. But when the concentration is increased to 12·5 mc. per sq. cm. radioactive phosphorus (^{32}P) appears in the blood 9 to 14 days after the application, and with a concentration of 25 mc. per sq. cm. ^{32}P appears in the blood within 2 to 4 hours.

The penetration of ^{32}P into the blood is due to damage of the epithelium by the beta rays emitted by the isotope, and is about twice as rapid with the lanolin ointment as with the watery solution. *A. Orley*

1359. **Mineral Metabolism in Rickets Studied by Means of Radioactive Isotopes.** (Изучение некоторых вопросов экспериментального рахита при помощи методики меченых атомов)
E. A. PERKOVICH. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 12–18, No. 3, May–June, 1956. 4 figs., 10 refs.

The disturbances of mineral metabolism observed in experimental rickets in rats are similar to those observed in spontaneous rickets in children in that there is a deficiency of calcium and phosphorus in the bones. By means of the radioactive isotopes of these two elements it was possible to establish that in rats the deficiency is caused by an intensification of mineral metabolism in the rachitic bones, with the result that although they assimilate mineral salts avidly, they are unable to retain them for any length of time.
A. Orley

1360. **The Effect of Radioactive Strontium on the Consolidation of Fractures.** (Влияние радиоактивных изотопов стронция на консолидацию перелома)
L. M. KAPITSA and A. D. FEDOROVA. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 18–21, No. 3, May–June, 1956. 5 figs.

It was shown in experiments carried out at the Order of Lenin Institute, Leningrad, that radioactive strontium, injected intravenously in cases of fracture of bone in animals, is mainly absorbed by the bone near the fracture and by the surrounding callus. The isotope, given in doses of 1·6 mc. per kg. body weight, stimulates the regeneration of bone tissue and accelerates the consolidation of the fracture. *A. Orley*

1361. ***In vitro* Studies on Human Synovial Membrane. A Metabolic Comparison of Normal and Rheumatoid Tissue**
J. T. M. DINGLE and D. P. P. THOMAS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] 37, 318–323, Aug., 1956. 4 figs., 7 refs.

1362. **Further Data on the Biochemistry of the Renin of Normal Kidneys and of Renol—a Pressor Substance in Rabbit Kidneys Rendered Ischaemic *in vivo* and Autolysed *in vitro*.** (Дальнейшие данные по биохимической характеристике ренина нормальных почек и ренола —прессорного вещества ишемизированных in vivo и автолизированных in vitro почек кролика)
O. A. STEPUN, A. I. LOMAURI, G. S. AKHMETELI, and V. N. CHIKVAIDZE. *Архив Патологии* [*Arkh. Patol.*] 18, 52–57, No. 2, 1956. 4 figs., 6 refs.

In biochemical investigations carried out at the Institute of Clinical and Experimental Cardiology, Tiflis, Georgia, the authors isolated a pressor substance from the ischaemic kidneys of rabbits by autolysis at *p*H 3·8 and at 37° C. This substance—which they designate " renol "—differs from renin in several respects; for example, it is not present to any extent in normal kidneys; also, whereas renin is destroyed by autolysis, the amount of renol increases during autolysis, reaching a maximum after about 10 hours and remaining active up to 48 hours. It does not convert hypertensinogen into hypertensin. The renal content of renol remains constant for 24 to 48 hours, that is, while it is being released from combination with protein. Whereas chemically renin is a single uniform substance, renol consists of two components—a thermolabile factor and a thermostable co-factor. The pressor effect is exerted only when both these fractions are present.
L. Crome

CHEMICAL PATHOLOGY

1363. **Tubeless Gastric Analysis. Evaluation of a Technic Using a Dye–Resin Compound**
M. L. SIEVERS and R. V. GIESELMAN. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] 1 (New Series), June, 1956. 1 fig., 15 refs.

Although the technique of tubeless gastric analysis with quininium cation-exchange resin differentiates fairly satisfactorily between normal gastric acidity and achlorhydria, it requires the use of expensive equipment for the estimation of quinine in the urine. In a report from the Veterans Administration Hospital, St. Louis, the authors describe the use of a new compound in which a dye, azure A, is coupled to the cation-exchange resin " amberlite XE-96 ". The dye is liberated in the presence of acid in the stomach and is then excreted in the urine, the urine passed during the 2 hours after the ingestion of 2 g. of the compound being compared visually with control urine and standards containing 0·0001% and 0·0002% of the dye. [For details of the procedure reference must be made to the original paper.] Caffeine sodium benzoate is used as a secretory stimulant rather than ethyl alcohol, which tends to elute the azure A from the resin.

A series of tests were performed on 93 patients (92 males), there being good agreement between the results obtained with azure A and quininium resins in 89·2% of initial tests. Repeated tests in cases giving equivocal results increased this proportion to 95·7%.

Gastric intubation was performed only when both tests gave negative results, as the authors state that "false positive results are infrequent with tubeless gastric analysis" [though they do not produce any evidence in support of this statement]. In 15 cases the results with both resins indicated achlorhydria, but in at least 6 these were shown to be false negative results.

It is claimed that the test is of value as a simple screening procedure for achlorhydria.

[Although this investigation was, in the abstracter's opinion, badly planned and imperfectly controlled, the results suggest that the method may be of limited usefulness.] *M. Sandler*

1364. **The Clinical Significance of Hyperglobulinemia. I. Diagnostic Implications. II. Correlation with Liver Function Tests, Serologic Tests for Syphilis, and Bone Marrow Examinations**

A. R. FEINSTEIN and R. G. PETERSDORF. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 899–924 and 925–937, May, 1956. 2 figs., bibliography.

In the first part of this study, the object of which was to determine the significance of the isolated laboratory finding of a raised serum globulin level, the authors, working at Yale University School of Medicine, analysed the hospital records of 394 patients in whom a serum globulin level of 3·9 g. per 100 ml. or higher had been noted. Of these patients 268 had diseases generally associated with an elevated serum globulin content, namely, multiple myeloma, sarcoidosis, collagen diseases, liver disease, cancer, chronic pulmonary disease, and certain infections. The remaining 126 were suffering from a variety of disorders not commonly associated with an increase in the serum globulin fraction, such as cardiovascular disease, renal disease, endocrine disorders, and musculo-skeletal diseases.

Of the patients in whom the serum globulin level exceeded 5 g. per 100 ml., over 90% had specific "hyperglobulinaemic" diseases, about half of them suffering from multiple myeloma, sarcoidosis, or collagen disease. Of those in whom the serum globulin level was between 4·2 and 5 g. per 100 ml., the majority had hepatic disease, metastatic carcinoma, or chronic diffuse pulmonary disease, only a few having multiple myeloma, sarcoidosis, or collagen disease. Lastly, those in whom there was a minimal rise in the serum globulin level (3·9 to 4·2 g. per 100 ml.) had a great variety of unclassified chronic diseases of one or more systems. These findings appear to indicate that a slight elevation of the serum globulin level is of very limited diagnostic significance, whereas a marked elevation frequently indicates a specific pathological process. The authors point out that only 20% of the patients with hyperglobulinaemia also had hyperproteinaemia, indicating that in the majority the pathological condition was associated with a fall in serum albumin level, exceptions being sarcoidosis and collagen disease, in which the serum albumin level was approximately normal despite the marked rise in the serum globulin level.

In the second part of this study the authors investigated the relationship between the serum globulin levels and the results of liver function tests, serological tests for syphilis, and bone-marrow examinations carried out on the same series of patients. Abnormalities in the liver function test results in 160 patients without overt hepatic disease were interesting in that they showed a positive correlation with the disturbances in the serum protein pattern. The cephalin–cholesterol flocculation reaction was more likely to be abnormal in the presence of a low serum albumin level, whereas the thymol reaction appeared more sensitive to elevation of the serum globulin level. In this group the thymol test gave a normal result more frequently than did the cephalin test, although both tests gave about the same number of abnormal results in patients with liver disease. Abnormal reactions to the cephalin and thymol tests were found more often in those diseases in which the raised serum globulin level was due mainly to an increase in the gamma-globulin fraction than in those in which there was an increase in all three globulin fractions or mainly in the alpha and beta fractions. The results of the alkaline-phosphatase and "bromsulphalein" retention tests showed no correlation with abnormal serum albumin or globulin values. However, there was abnormal retention of bromsulphalein in many of the patients without liver disease.

False positive reactions to serological tests for syphilis were observed in 4% of patients and were unrelated to the diagnosis of the condition or the serum globulin level. "Benign" plasmacytosis was found in 15 and a diagnosis of multiple myeloma established or confirmed in 12 of the 71 patients in whom bone-marrow examination was performed.

The authors' findings are compared with those reported in the literature. *Victor M. Rosenoer*

1365. **The Blood Pyruvic Acid Level in Renal Diseases and in Uraemic Coma**

J. KLEEBERG and S. GITELSON. *Journal of Clinical Pathology* [*J. clin. Path.*] **9**, 148–152, May, 1956. 1 fig., 33 refs.

The significance to be attached to an increase in the blood pyruvic acid level in the presence of renal disease is discussed in this paper from the Rothschild Hadassah University Hospital, Jerusalem. Normal values (0·5 to 1·1 mg. per 100 ml.) were found in 24 out of 26 patients with uncomplicated nephritic conditions and chronic urinary infections, including patients with severe acidosis and others in uraemic coma. Similarly in 15 cases of essential hypertension, a condition which may eventually lead to renal failure or to complications causing hyperpyruvicaemia, the blood pyruvic acid level was normal. A raised pyruvic acid level was found in 4 out of 5 patients with renal disease accompanied by severe complications such as cerebral haemorrhage, hypertensive encephalopathy, and pulmonary oedema, as well as in 6 patients in coma due to cerebral haemorrhage or embolism and in 8 in hepatic coma, in whom there was no evidence of failure of renal function. These results indicate that renal disease itself does not raise the blood pyruvic acid level. This, the authors consider, is to be expected, having regard to the relatively minor part

played by the kidneys in the pyruvic acid metabolism of the body and the small amount of pyruvic acid excreted in the urine. Even in severe uraemic states the low alkali reserve was not accompanied by any change in the blood pyruvic acid level.

It is suggested that the level of pyruvic acid in the blood may be of value in the differential diagnosis of various types of coma. The mean blood pyruvic acid level in the 18 patients with hyperpyruvicaemia was in the neighbourhood of 2·3 mg. per 100 ml. (range 0·8 to 6·5 mg. per 100 ml.). *Harry Coke*

1366. **Vasopressin Tannate in Oil and the Urine Concentration Test**

H. E. DE WARDENER. *Lancet* [*Lancet*] **1**, 1037–1038, June 30, 1956. 1 fig., 4 refs.

In view of the potential dangers of strict water deprivation and the limitations and unpleasantness of tests of the kidney's maximum ability to concentrate urine, the author, at St. Thomas's Hospital, London, investigated further the possibility of substituting an injection of vasopressin tannate in oil for a long period of water deprivation. Fluid, which was taken to include soups, ice-cream, and fruit, was withheld from 27 patients convalescent from renal disease and 18 convalescent from non-renal disease for 36 hours and from 17 healthy subjects for 48 hours. The urine tested was that passed in the last 8 hours of this period of deprivation. The effect of injecting vasopressin was observed 1 to 2 weeks later; a subcutaneous injection of vasopressin tannate in oil was given at 7 a.m. and the urine passed between noon and 8 p.m. tested, no limitations being placed on the intake of food or drink. The osmolar concentration of the urine was calculated from the depression of the freezing point.

The results showed that the concentration of urine following fluid deprivation was slightly greater than after injection of vasopressin, but the difference became less as the osmolarity of the urine approached that of plasma (a difference of 0·002 at a specific gravity of 1·022). The reproducibility of the vasopressin method was satisfactory—the standard deviation in three tests on 9 healthy subjects being 82 milli-osmoles per litre. The author states that no comparable figures for repeated water deprivation tests were available. He points out that since the effect of vasopressin tannate in oil on the urine concentration lasts for 24 hours it is necessary only to measure the specific gravity of all urine samples passed in the 24 hours following the injection.

No complications, apart from some torpor in the healthy subjects, were noted. The chief disadvantage of the method is that the vasopressin tannate in oily suspension requires warming and shaking before use, and a large bore needle has to be used.

The author concludes that when an estimate of the kidney's maximum ability to concentrate urine is needed, injection of vasopressin tannate in oil can justifiably be substituted for a long period of fluid deprivation. Moreover, with vasopressin the test can be carried out frequently—for example, weekly—thus greatly increasing its value. *Victor M. Rosenoer*

1367 (*a*). **A Calcium-infusion Test. I. Urinary Excretion Data for Recognition of Osteomalacia**

B. E. C. NORDIN and R. FRASER. *Lancet* [*Lancet*] **1**, 823–826, June 2, 1956. 4 figs., 10 refs.

1367 (*b*). **A Calcium-infusion Test. II. "Four-Hr. Skeletal Retention" Data for Recognition of Osteoporosis**

J. M. FINLAY, B. E. C. NORDIN, and R. FRASER. *Lancet* [*Lancet*] **1**, 826–830, June 2, 1956. 4 figs., 11 refs.

In the first of these two papers the authors describe a standard procedure for a calcium-infusion test which they have employed at the Postgraduate Medical School of London in the investigation of known or suspected cases of metabolic bone disease, and report the findings for urinary calcium excretion in patients with osteomalacia. The patients to be tested were kept for 3 days before and also throughout the test on a diet containing 100 to 150 mg. of calcium and 500 to 700 mg. of phosphorus. On the fourth day they received an intravenous infusion of calcium gluconate calculated to supply 15 mg. of calcium per kg. body weight. The urine was collected for 24 hours on the previous day and for 12 hours on the test day, the net output of calcium after infusion being expressed as a percentage of the dose given after deduction of basal excretion calculated from the previous 24 hours' urinary calcium output.

A total of 98 patients were studied. In 21 "normal" patients the net 12-hour urinary calcium excretion was 33 to 53% of the dose administered (mean 41±7%). In 12 cases of proved osteomalacia with a manifest cause the highest value was 26·8% and the lowest 1·5%, with a mean of about 15%; there was no correlation between the amount of calcium excreted and the severity of the disease. In 17 cases of steatorrhoea without definite osteomalacia the results varied considerably, being normal in 7 cases, low (below 27%) in 8, and high in 2. In 30 cases of miscellaneous disease there were 10 false positive results, but these were attributable to such causes as renal failure in all except 4. The authors suggest that in doubtful cases the test may provide additional evidence for or against a diagnosis of osteomalacia.

In the second paper the authors show that the calcium-infusion test described above failed to differentiate between osteoporotic and "normal" patients. In an attempt to make this distinction they measured not only the net calcium output in the urine, but also the excess calcium still circulating in the extracellular space, that fraction of the calcium not found in either pool being assumed to be bound in the skeleton. In this way the "4-hour skeletal retention" of calcium was calculated. In 10 patients without osteomalacia this was 50 to 62% of the dose; in 8 cases of osteomalacia skeletal retention was above the normal range, while 11 out of 15 patients with osteoporosis retained less than 50% of the administered dose, the retention in the remaining 4 being within the normal range. In almost all cases the "4-hour skeletal retention" and the 12-hour urinary excretion of calcium together accounted for 95% of the infused dose; the authors assumed [on good grounds] that the fraction lost in the faeces was insignificant. They conclude that the calcium retention test "may offer a biochemical criterion for osteoporosis". *C. L. Cope*

HAEMATOLOGY

1368. **L.E. and L.E.-like Cells: a Morphological Study**
E. N. GOULDIN and L. W. DIGGS. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **49**, 560–566, June, 1956. 6 figs., 25 refs.

The sequence of changes occurring in the nucleus during formation of the L.E. cell were observed in smears of the buffy coat of defibrinated blood of patients with systemic lupus erythematosus, the smears being taken at 15-minute intervals after collection. Many variations in the pattern were noted, and when the nuclear alteration was focal, not generalized, the resulting inclusion body tended to be lumpy or flaky. The authors state that L.E.-like cells differ from typical L.E. cells in that the inclusion bodies are unevenly stained and have residual chromatin structures; they often have prominent and dark margins.

In 13 patients with systemic lupus erythematosus and 8 controls the numbers of L.E. cells, L.E.-like cells, and rosettes per 1,000 neutrophils in preparations from bone marrow or peripheral blood were recorded. As regards the controls, the number of L.E.-like cells varied, rosettes were present in half of them, and in one patient suffering from rheumatoid arthritis L.E. cells were found. In the authors' view the L.E. cell is not specific for systemic lupus erythematosus, but "the reliability of the diagnosis is increased in proportion to the number of typical L.E. cells seen". They suggest that a quantitative report on the results should be given whenever the L.E. test is performed. *E. G. Rees*

1369. **Effect of a Meal of Eggs and Different Fats on Blood Coagulability**
J. R. O'BRIEN. *Lancet* [*Lancet*] **2**, 232–234, Aug. 4, 1956. 2 figs., 6 refs.

The effect on the coagulability of the blood of feeding 50 g. of butter, margarine, or a proprietary vegetable cooking fat, or 2 boiled hen's eggs was investigated in 8 male afebrile patients aged 49 to 83. The test substances were added to a fat-free basic meal of unlimited toast, marmalade, and tea (with very little milk), and 1½, 3, and 4 hours after this meal estimations were made of the "'stypven' clotting time" (that is, the plasma clotting time accelerated by Russell's viper venom) which, as the author has previously shown, varies proportionately with the amount of thrombin generated in platelet-poor plasma and also with the silicone clotting time of whole blood.

Ingestion of all the test substances shortened the stypven clotting time. Although the 2 eggs contained only about 10 g. of fat, they produced a similar or even greater shortening of the clotting time. In view of the relatively high phospholipid content of eggs and of the author's observations on the effect of a preparation of pure egg phosphatidyl ethanolamine on the stypven clotting time, he concludes that although some of the effect on blood coagulation may be due to an increase of fatty acids in the plasma, it is probably due mainly to an increase in phospholipids such as phosphatidyl ethanolamine. *A. Brown*

MORBID ANATOMY AND CYTOLOGY

1370. **Cerebral Complications in Embryopathia Rubeolosa.** [In English]
J. A. KAPPERS. *Folia psychiatrica, neurologica et neurochirurgica Neerlandica* [*Folia psychiat. (Amst.)*] **59**, 92–110, April, 1956 [received July, 1956]. 10 figs., 26 refs.

After reviewing the previously recorded cases of rubellar embryopathy in which there were clinical or pathological signs of cerebral impairment, the author reports, from the University of Groningen, the structural findings in a foetus resulting from a spontaneous abortion which occurred at the 7th week of gestation, the mother having contracted unmistakable rubella during the 5th week of pregnancy.

The foetus showed neural abnormality of the telencephalon, metencephalon, diencephalon, and rhombencephalon which was characterized by excessive folding of the pallium with areas of excessive epithelial growth and focal necrosis. Some of the blood vessels were thickened and showed endothelial hyperplasia, and there was also some dorsal herniation of the brain through a gap in the cranium. The eyes and somatic organs were normal for the age of the foetus.

The author concludes that severe maternal rubella in the first 3 months of gestation may lead, if the foetus survives, to malformation of the brain, which is probably due to embryonic encephalitis, possibly with leptomeningitis, as the result of transplacental infection.
L. Crome

1371. **The Morphology and Pathogenesis of Coronary Atherosclerosis and its Significance in the Evolution of Secondary Myocardial Changes.** (О морфологии и морфогенезе коронарного атеросклероза и значении его в развитии вторичных изменений миокарда)
K. G. VOLKOVA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 12–18, No. 5, May, 1956. 13 refs.

Atherosclerosis of the coronary arteries begins with the appearance of lipid substances in the intima during the second decade of life. Small focal deposits appear first of all in the anterior descending branch of the left coronary artery near to its ostium, and later (at the end of the second or early in the third decade) in its circumflex branch and in the right coronary artery. The lipids (chiefly cholesterol and its compounds) enter the arterial wall from the blood stream by imbibition, passing from within outwards, and are partly carried away by the lymphatics of the external coat and partly deposited in the fibrous tissue of the intima, this deposition being favoured by the relative thickness of this layer in the coronary arteries. After the third decade thickening of the connective tissue on the inner side of the lipid deposits occurs and in the course of time thick, fibrous, atherosclerotic plaques are formed. The process spreads distally from the ostia of the branches of the coronary arteries towards their finer distal arborizations. In the sixth or seventh decade lipid macrophages, crystals of cholesterol, saponified lipid, and granular or continuous layers of calcification are found. Degeneration of the media then takes place, leading to its complete dis-

appearance, and the lumen of the vessel becomes narrowed by the projecting atheromatous plaques. As the formation of the atheromatous plaque proceeds, fine capillaries form in the outer and middle coats of the artery. Haemorrhages may occur around the vessels or in the vessel walls, but the author has rarely seen such cases as have been described by others, in which occlusion of the vessel results from the haemorrhage itself. It must be realized, however, that very little bleeding is required to occlude completely a vessel already narrowed by atheromatous plaques. More commonly ulceration of the plaque occurs from degenerative change, with penetration of blood into the wall of the vessel, thus occluding it lower down, or occlusion may result from thrombosis on the surface of the degenerating plaque.

It is pointed out that when coronary occlusion occurs in an atherosclerotic subject the possibility of an adequate collateral circulation being established must be lessened by the presence of atheroma in other branches of the coronary arteries, and that the results of experiments on healthy animals in which the effects of ligation of a branch of one of the coronary arteries are studied are not necessarily applicable to such subjects.

L. Firman-Edwards

1372. **The Pathology of Honeycomb Lung**

A. G. HEPPLESTON. *Thorax* [*Thorax*] **11**, 77–93, June, 1956. 26 figs., 48 refs.

Lung tissue from 66 cases of "honeycomb lung", as described by Oswald and Parkinson (*Quart. J. Med.*, 1949, **18**, 1; *Abstracts of World Medicine*, 1949, **6**, 201), was examined by the author at the Welsh National School of Medicine, Cardiff. The ages of the patients, 50 of whom were males, ranged from 5 months to 86 years, but only 5 were children and 53 were more than 50 years old. The preponderance of males was due to the inclusion of 32 coal-workers. Honeycomb lung was regarded as the primary or an important cause of death in 20 cases.

Diffuse and circumscribed forms are described, and evidence is given to show that the condition is always acquired rather than congenital. Obliteration of the terminal non-respiratory and respiratory bronchioles and their subdivisions is regarded as the primary change. The most important cause of this in the present series was fibrosis (53 cases), which may have followed pneumonia or focal collapse in some cases, though in the majority the findings were non-specific; the remaining 13 cases showed signs of a more specific cause, such as eosinophilic granuloma (4 cases), berylliosis (2), sarcoidosis (1), tuberculous pneumonia prolonged by therapy (3), scleroderma (2), leiomyomatosis (1), and giant-cell pneumonia (1). As a result of the obliteration, bronchioles in the neighbouring unaffected lung parenchyma dilate to form cystic spaces, which may enlarge progressively owing to secondary valvular obstruction of communicating bronchioles.

Attention is drawn to the hyperplasia and hypertrophy of smooth muscle which occur in this and other fibrosing pulmonary diseases and are regarded as a compensatory mechanism to encourage expulsion of air from the cysts. Tuberous sclerosis, in which honeycomb lung associated with hyperplasia of the smooth muscle occurs, must be considered in the differential diagnosis, but there was no evidence of this condition in the 50 cases in this series in which full details of the necropsy were available.

The cystic spaces are commonly lined by epithelium derived from the bronchioles, and the excessive degree of proliferation of this epithelium which sometimes occurs must be distinguished from the proliferation due to primary pulmonary adenomatosis, which may itself conceivably produce a honeycomb pattern. In none of the author's cases had the epithelial proliferation become malignant.

[The accompanying illustrations are excellent.]

T. Bird

1373. **Carcinoma of the Bronchus**

C. RAEBURN and W. W. WALTHER. *Lancet* [*Lancet*] **1**, 778–779, May 26, 1956. 5 refs.

Although three main types of carcinoma of the bronchus—the oat-cell, the squamous-cell, and the adenocarcinoma—are recognized in most systems of histological classification under these or other names, a group of undifferentiated tumours remains which are variously described as "mixed", "large-cell", "polygonal-cell", or "squamoid". This group accounted for 21% of a series of 171 post-mortem specimens examined by the authors at the Area Laboratory, Whipps Cross Hospital, London, and classified in the manner described by Walter and Pryce (1955), in whose series only 10·7% were so classified. By staining sections of these "polygonal-cell" tumours for mucin, however, this figure could be reduced to 14%, 12 of the 36 tumours being shown to contain mucin and therefore being reclassified as adenocarcinomata. The corrected figure for the latter group was 22·8% instead of 15·8%, and was thus more nearly in agreement with that of Walter and Pryce (28·3%).

[The importance of staining for mucin in all cases of carcinoma of the lung was, in fact, insisted upon by Walter and Pryce.]

D. M. Pryce

1374. **Cancer Diagnosis by Bone Marrow Smears**

C. H. JAIMET and H. E. AMY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 617–629, April, 1956. 10 refs.

To determine the value of examination of bone-marrow smears in the diagnosis of cancer, the authors, at the General Hospital and St. Joseph's Hospital, Hamilton, Ontario, studied bone-marrow aspirates obtained from more than 4,100 patients, the technique used having been described previously (Amy and Jaimet, *Canad. med. Ass. J.*, 1953, **69**, 424). Smears prepared from concentrated marrow cells and direct smears from the mixed aspirate were made as a routine, but were studied only when marrow-particle imprints or smears could not be obtained. By a similar procedure imprints from lymph nodes and, for the purposes of comparison, from tumour sites were prepared. To assist in distinguishing abnormal marrow cells from malignant cells the authors examined over 200 specimens of bone marrow from

patients who were free from malignant disease and also marrow aspirates taken from 128 patients on admission to hospital—that is, before clinical examination.

The authors state that " by the study of the normal we have learned to recognize early abnormalities, and malignant disease being one with such protean manifestations, we continually find first evidence of it in marrow imprints ". Further, by the procedure described they are finding " increasing evidence of cancer in a large numer of patients who heretofore resisted diagnosis by all other means ". The tendency of tumour cells to form " cell-balls " or metastatic clumps renders them easily distinguishable from the cells of the normal bone marrow. The nuclei of the former appear vesiculated, and their nucleoli vary in size, number, and shape. However, the authors state that they " have not yet designated any common denominator by which a cell that occurs singly in the marrow can be definitely tagged as a carcinoma cell when it occurs alone and isolated in a marrow preparation; nor can one indicate with high correctness the site of its primary origin ". Nevertheless single malignant cells usually exhibit features which distinguish them from surrounding haematopoietic cells.

From a study of the action of some antimetabolites on cell growth it is concluded that " there is a difference in the anabolism of nucleic acids in cells of different origins which demonstrated selective action for specific therapeutic compounds ". *R. J. Ludford*

1375. **Morphological Changes in the Diaphragm in Inflammatory Conditions of the Peritoneal and Pleural Cavities.** (Морфологические изменения диафрагмы при воспалительных процессах в брюшной и плевральных полостях)
Y. P. ARGUNOVA. *Архив Патологии* [*Arkh. Patol.*] **18**, 83–86, No. 1, 1956. 5 figs., 12 refs.

The histology of the diaphragm was studied post mortem in 17 cases of peritonitis and pleurisy. Marked changes were found, particularly affecting the neural structures, which showed fragmentation and destruction of the motor end-organs. Muscle fibres showed degenerative changes. The lymphatics provided the main channels for the spread of infection across the diaphragm. In all cases of peritonitis there was either frank pleurisy or an inflammatory reaction in the diaphragmatic pleura. *L. Crome*

1376. **The Interrelationship of the Fibrous Elements of Connective Tissue in the Light of New Data on the Structure of Collagen.** (Взаимоотношение волокнистых структур соединительной ткани в свете новых данных о строении коллагема)
G. V. ORLOVSKAYA. *Архив Патологии* [*Arkh. Patol.*] **18**, 68–74, No. 1, 1956. 33 refs.

The present communication, one of a series of reports on a study of the histochemistry, electron microscopy, and diffraction radiography of collagen, describes the histochemical properties of the residue after the extraction of carbohydrates from collagen with a 0·1 M solution of disodium phosphate at *p*H 9, followed by the removal of globular protein with 5% sodium chloride solution and of procollagen with a citrate buffer at *p*H 4. This residue, which has been given the name of " collastromin " by the author, contains sulphated mucopolysaccharides which are rendered more demonstrable histochemically by the removal of the procollagen. It was also noted that argyrophil fibres became visible in the material.

The author discusses the application of these findings to certain problems in pathology, for example, those of fibrinoid degeneration. The argyrophil fibres visible in fibrinoid tissue are considered to represent a protein of collastromin rendered visible by the replacement and removal of procollagen. *L. Crome*

1377. **Analytical Pathology. III. New Observations on the Pathogenesis of Glomerulonephritis, Lipid Nephrosis, Periarteritis Nodosa, and Secondary Amyloidosis in Man**
R. C. MELLORS and L. G. ORTEGA. *American Journal of Pathology* [*Amer. J. Path.*] **32**, 455–499, May–June, 1956. 28 figs., 20 refs.

At the Sloan–Kettering Institute and the Memorial Center for Cancer and Allied Diseases, New York, the authors have applied the methods described in detail in earlier papers (*Lab. Invest.*, 1955, **4**, 69, *Amer. J. Path.*, 1955, **31**, 687; *Abstracts of World Medicine*, 1955, **18**, 346, and 1956, **19**, 90) to the investigation of certain renal diseases. The serum globulin of rabbits immunized against human globulin was coupled with fluorescein, and sections of normal and diseased kidneys obtained from human subjects at necropsy treated with the fluorescein–globulin conjugate. It was shown by specific absorption and blocking tests that any fluorescence resulting in the sections was due to the presence of human γ globulin.

The ratio of glomerular to tubular fluorescence, measured photometrically, averaged 1·2 in 16 control subjects. (Only 3 of these kidneys were histologically normal, the others showing nephrosclerosis, pyelonephritis, or other lesions.) Increased fluorescence of the glomerular capillary walls increased the ratio to between 1·9 and 2·8 in cases of lipid nephrosis (1), combined acute and subacute glomerulonephritis (2), acute glomerulonephritis (4), and renal amyloidosis (1), while in a case of periarteritis nodosa with acute nephritis the ratio was raised both in the glomeruli and in the vicinity of necrotic arteries.

It is concluded that in the diseases investigated γ globulins are deposited in the glomeruli, and the theory is advanced that these are, at least in part, antibodies against antigens which have become fixed there, the pathogenesis of these conditions being of an " immunoallergic " nature.

[Although their findings are suggestive, the authors have in fact done no more than demonstrate the deposition of γ globulin in the glomeruli in certain diseases. It has yet to be shown that this is due to the presence of antibodies against particular antigens and not to local, non-immunological changes favouring nonspecific accumulation of γ globulin.]
M. C. Berenbaum

Microbiology and Parasitology

BACTERIA

1378. **The Mechanism of the Action of Botulinus Toxin on Respiration.** (К механизму действия ботулинического токсина на дыхание)
V. N. Abrosimov. *Архив Патологии* [*Arkh. Patol.*] **18**, 86–92, No. 1, 1956. 2 figs., 12 refs.

Experiments were performed on rabbits, cats, and kittens to determine the primary locus of the action of botulinus toxin. Before and after the introduction of the toxin the threshold of excitability of the vagus, sciatic, and phrenic nerves was measured, and the effect of faradic stimulation of the latter on respiration was observed. It was found that the site of action of the toxin is not peripheral but central, and it was concluded that the toxin acts directly upon the respiratory centre.
L. Crome

1379. **Growth of *Mycobacterium tuberculosis* in Liquid Media**
I. L. Miller and W. G. Roessler. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 716–725, May, 1956. 7 figs., 18 refs.

A study has been made of the effects of agitation on growing cultures of *Mycobacterium tuberculosis*. Contrary to some reports in the literature, growth of the organism is more rapid and greater cell numbers are obtained in shaken than in stationary cultures. Generation times obtained in a serum-albumin–"tween" medium with strain 198ARB were 17·8 and 25·3 hours, respectively, for cultures shaken and stationary; comparable results obtained with strain H37Rv were 17·9 and 20·5 hours. Generation times obtained with strain 198ARB in a tween medium without serum albumin were 19·6 and 24·8 hours, respectively, for cultures shaken and stationary; comparable results obtained with strain H37Rv were 21·0 and 25·4 hours.—[Authors' summary.]

1380. **Cultures of Tubercle Bacilli on Media Containing Blood from Different Species.** (Cultures du bacille de Koch sur milieux au sang de diverses espèces)
H. Hinglais, M. Hinglais, and M. Langlade. *Presse médicale* [*Presse méd.*] **64**, 910, May 16, 1956. 5 refs.

In the laboratories of the Paris Faculty of Medicine bovine and human strains of *Mycobacterium tuberculosis* were cultured on three different media containing human, rabbit, and rat blood respectively. These were prepared by adding to 8 volumes of the base (2% nutrient agar containing 1% glycerin) 2 volumes of sterile blood with acid–citrate–dextrose solution as anticoagulant.

Many colonies of the human strain appeared by the 10th day on the media containing human and rabbit blood, but none had appeared on the rat-blood medium even after 90 days. When the bovine strain was inoculated, a few colonies were present on the media containing human and rabbit blood on the 10th day and many colonies had appeared by the 20th day, whereas on the rat-blood medium no colonies were present on the 12th day, a few were present on the 20th day, and many had appeared by the 30th day. Rat blood seems, therefore, to inhibit the growth of the human strain, but not to affect the bovine strain significantly. The experiments were repeated 3 times with blood from different sources, with identical results. [However, no experiments are reported in which different strains of human and bovine tubercle bacilli were used.] *M. Lubran*

1381. **A Comparative Study of Laryngeal Swabs and Gastric Lavage in the Detection of Tubercle Bacilli**
J. I. Tonge and P. G. Hughes. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 930–939, June, 1956. 10 refs.

A comparison of the results obtained by gastric lavage and laryngeal swabbing in the detection of tubercle bacilli in cases of pulmonary tuberculosis was made over a period of one year in 465 patients attending the Chest Clinic of the Queensland State Health Department, Brisbane. The patients included a number with newly diagnosed pulmonary tuberculosis, mostly detected radiologically, while others with proved infection were attending for routine post-treatment examination or for confirmation of activity for pension purposes.

Both techniques were used in every case, and where possible on three separate occasions, a grand total of 1,305 pairs of examinations being made. The laryngeal swabs were taken with a No. 14 gauge stainless steel wire tipped with cotton wool. On receipt in the laboratory the swab was washed in 1·5 ml. of 2% sodium hydroxide solution, which was allowed to stand for 30 minutes and then neutralized with 2·5 N hydrochloric acid and centrifuged. The deposit was mixed with 0·1 ml. of a penicillin solution containing 2,000 units per ml. and then inoculated on to Löwenstein–Jensen medium and incubated at 37° C. for 6 weeks. The gastric contents (or washings with sterile water) were collected in a dry sterile container, an equal volume of 4% sodium hydroxide solution being added on arrival in the laboratory, and the specimen agitated violently for 10 minutes. The rest of the procedure was the same as for the laryngeal swabs.

Positive cultures were obtained by both methods on at least one occasion from 52 (11·2%) of the 465 patients, and negative cultures on all occasions from 333 (71·6%). Positive cultures were obtained by gastric lavage alone from 78 (16·8%) and by laryngeal swabbing alone from only 2 (0·4%). Of the 1,305 pairs of examinations performed, 7·1% gave positive and 79% negative results by both methods, in 13·4% only the gastric culture was positive, and in 0·5% only the laryngeal culture was positive. Of 111 cases in which 3 specimens of each type were examined and a positive result obtained by

both methods, all 3 gastric cultures were positive in 54 and all 3 laryngeal cultures in only 16. In 93 cases in which both specimens collected on the same day gave positive cultures, growth occurred more rapidly and was more dense in the gastric cultures; of the 372 slopes inoculated from gastric specimens (4 from each) growth occurred on 341 (92%), while of those inoculated from laryngeal specimens growth occurred on only 275 (74%). The contamination rate for gastric lavage was 7·9% and that for laryngeal swabs 0·31%.

The authors conclude that " a single gastric lavage [is] almost twice as effective as three laryngeal swabs in obtaining cultures positive for *Mycobacterium tuberculosis* ". *I. M. Librach*

1382. ***Bacteroides* in Intra-abdominal Sepsis. Their Sensitivity to Antibiotics**

W. A. GILLESPIE and J. GUY. *Lancet* [*Lancet*] **1**, 1039–1042, June 30, 1956. 37 refs.

In a study carried out at the Royal Infirmary, Bristol, of the micro-organisms associated with intra-abdominal sepsis organisms of the *Bacteroides* group were isolated on 67 occasions from 111 specimens of pus from cases of localized or generalized peritonitis. Many of the strains cultured were associated with other organisms, the most common being coliform bacilli, and anaerobic and aerobic streptococci. The sensitivity of these *Bacteroides* strains was determined to the following antibiotics: penicillin, streptomycin, chloramphenicol, oxytetracycline, chlortetracycline (aureomycin), tetracycline, erythromycin, bacitracin, neomycin, and polymyxin B. Sensitivity to bacitracin, neomycin, tetracycline, and chlortetracycline was determined by the disk method alone, and that to polymyxin B by a quantitative (doubling dilution) method only, the drugs being incorporated in the growth medium. Sensitivity was also determined to sulphadiazine. The majority of the *Bacteroides* were grown anaerobically in jars containing hydrogen and 5% carbon dioxide, previous experiments having shown that these conditions did not interfere with the activity of the antibiotic under test. It was also shown that the results obtained by the disk technique and the quantitative dilution technique were in good agreement.

All the strains tested were sensitive to the tetracyclines and chloramphenicol, most of them to sulphadiazine, and more than half were fully or moderately sensitive to erythromycin. On the other hand most strains were resistant to penicillin and streptomycin, and all those tested against bacitracin, neomycin, and polymyxin B were resistant to these substances. Because penicillin and streptomycin are frequently given simultaneously an attempt was made to determine whether these drugs could in fact enhance each other's action to a degree which would make them clinically effective in infections due to *Bacteroides*. Cultures of 10 different strains were therefore made on blood agar containing various concentrations of penicillin and streptomycin. These showed that the presence of a subinhibitory concentration of either drug did not increase the sensitivity to the other more than twofold. Because intra-abdominal sepsis is often associated with more than one type of organism the choice of a suitable antibiotic may present certain difficulties. Since the majority of coliform bacilli and streptococci are also sensitive to the tetracyclines it would appear that the " broad spectrum " antibiotics such as the tetracyclines should produce the most favourable results in cases of intra-abdominal sepsis. But the authors recall that these drugs, like other antibiotics, are associated with certain risks, and therefore should not be used in conditions in which antibiotics are not needed, such as uncomplicated appendicitis. They also point out that the sensitivity tests described were performed with organisms of intestinal origin, and that organisms of different origin may differ in their sensitivity, particularly to penicillin, as shown by Garrod. *R. F. Jennison*

SEROLOGY AND IMMUNOLOGY

1383. **A New Intradermal Antigen for the Diagnosis of Schistosomiasis**

A. F. SHERIF. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **50**, 105–112, June, 1956. 3 figs. 15 refs.

From the University of Alexandria the author reports a method for the preparation of a diagnostic antigen from miracidia obtained from ova excreted in the urine by patients with schistosomiasis, newly infected and untreated cases being preferred and large volumes of urine used. The eggs are separated from urine by filtering successively through two sieves of fine silver-wire mesh, the first with apertures of 150 μ to separate off extraneous matter and the second with apertures of 40 μ which retains all the ova and a few crystals. The funnel containing the second sieve is attached to a suction pump. The filtrate is washed with saline and the ova suspended in 10 ml. of saline and centrifuged for 5 minutes at 750 r.p.m. The supernatant is then replaced by tap-water and the ova incubated at 37° C. for 10 minutes, when about 80% of the ova will have hatched. An equal volume of 96% alcohol is then added to kill the miracidia, the suspension centrifuged for 2 minutes at 3,000 r.p.m., the supernatant decanted, and the residue resuspended in a few drops of 96% alcohol. It is then transferred to a sterile vessel, dried under vacuum, and the dried residue pulverized and weighed. A 1% suspension of the powder in sterile saline is then made, left 48 hours in a refrigerator with occasional shaking, centrifuged for 5 minutes at 3,000 r.p.m., filtered through a Seitz filter, and an equal volume of 0·8% phenol in saline added. The final solution is therefore made up of 0·5% antigen (dry weight) in 0·4% phenol in saline. This is transferred to sterile ampoules and kept in a refrigerator. For use a 1-in-10 dilution of the stock antigen is made immediately before use and 0·25 ml. injected intradermally into one forearm, 0·25 ml. of 0·4% phenol in saline being injected into the other arm as a control.

The miracidia used by the author were mostly obtained from the eggs of *Schistosoma haematobium*, with about

1% from *S. mansoni*. In trials on 470 persons known to be infected with schistosomiasis a positive reaction (a weal at least 10 mm. in diameter surrounded by an erythematous flare developing within 20 minutes) was obtained in every case, whereas among 474 persons known to be free from schistosomiasis negative reactions were obtained even in cases of allergic disease or infection with protozoa, nematodes, or cestodes. Patients who had completed a full course of antischistosomal treatment all gave negative reactions to the antigen 3 to 6 months after completion of treatment. Others tested after 1 to 3 months still gave positive reactions.

I. M. Rollo

1384. **A Study of C-reactive Protein in the Serum of Patients with Congestive Heart Failure**

S. K. Elster, E. Braunwald, and H. F. Wood. *American Heart Journal* [*Amer. Heart J.*] **51**, 533–541, April, 1956. 14 refs.

At the Mount Sinai Hospital, New York, the blood of 50 adults suffering from heart disease of various types complicated by congestive failure was tested with specific antiserum for the presence of C-reactive protein. A single blood sample only was taken from 10 ambulatory patients with non-progressive congestive heart failure and in none of these was the protein found. Serial examinations were carried out on the remaining 40 patients, of whom 30 gave a positive reaction at some stage. Generally, the occurrence of C-reactive protein in the blood was associated with the more severe degrees of heart failure, and in 16 cases it disappeared from the blood with the patient's recovery.

The presence of C-reactive protein could be attributed to active rheumatic heart disease in 4 cases, acute myocardial infarction in 2, and to subacute bacterial endocarditis in one, but in the remaining 23 cases (consisting of 11 cases of inactive rheumatic heart disease, 11 of hypertensive and arteriosclerotic heart disease, and one of syphilitic heart disease) its presence was apparently attributable only to the congestive heart failure. The 10 patients without C-reactive protein showed no significant difference in age, sex, colour, circulation time, venous pressure, or the presence or absence of hepatomegaly, oedema, pyrexia, or leucocytosis from those with the protein. The erythrocyte sedimentation rate was increased and pulmonary rales were present more commonly in the latter than in the former group.

The authors conclude that the association of C-reactive protein with congestive heart failure limits the value of the test as a measure of rheumatic activity or of myocardial necrosis after infarction. *M. Lubran*

1385. **Poliomyelitis-virus Flocculation by a Micromethod**

W. Smith, F. W. Sheffield, G. Churcher, and L. H. Lee. *Lancet* [*Lancet*] **2**, 163–165, July 28, 1956. 1 fig., 1 ref.

The authors recently reported (*Lancet*, 1956, **1**, 710) the occurrence of a type-specific virus-antibody flocculation reaction with poliomyelitis virus. They now describe, from University College Hospital Medical School, London, a microtechnique for carrying out this reaction, which is as follows. After dilution with dropper pipettes calibrated to deliver 50 drops of saline per ml., one drop of diluted antiserum is mixed with one drop of concentrated flocculating antigen, diluted if necessary, against each virus type in Dreyer agglutination tubes, the total volume being 0·4 ml. To prevent evaporation during incubation the agglutination tubes are kept in a simple humidity chamber (described) which is placed in an ordinary bacteriological incubator. The period of incubation is usually 2 to 4 hours at 37° C., but no deleterious effects on the reaction have been observed in tubes incubated for 24 hours, provided evaporation has not occurred.

For examination for flocculation a small drop from each tube is transferred with a platinum loop to a coverslip and examined by low-power dark-ground microscopy as a hanging-drop preparation. In a good positive reaction the floccules consist of lattices of varying size and the reaction can be read at a glance, but in titrations the aggregates become progressively smaller so that a fine end-point is difficult to ascertain. Only tentative conclusions can be drawn so far, but it appears that the Leon strain of virus (Type 3) can be rendered non-infective by heat treatment (56° C. for 30 minutes) without appreciably affecting its flocculating antigen, but the flocculating antigen of the Brunhilde (Type 1) and Y-SK (Type 2) strains is destroyed by heating. To render these latter strains non-infective, the use of formalin has been tried and has given encouraging results. The authors point out that the micromethod described is economical of reagents, is simple and rapid to perform, and is sufficiently accurate for most purposes. *A. Ackroyd*

1386. **Poliomyelitis Vaccine Studies**

G. C. Brown, A. S. Rabson, and D. E. Craig. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **71**, 604–611, June, 1956. 5 figs., 15 refs.

In an investigation carried out at the University of Michigan School of Public Health, Ann Arbor, into whether previous passive immunization conferred by the administration of gamma globulin interferes with the artificially acquired active immunity produced by poliomyelitis vaccine, 27 boys aged 8 to 10 years were injected intramuscularly with 0·28 ml. of gamma globulin per lb. (0·6 ml. per kg.) body weight 3 days before the first of three intramuscular injections each of 1 ml. of poliomyelitis vaccine, the second injection being given one week later and the third 5 weeks later.

Neutralization tests performed on blood samples taken 2 weeks after the last injection showed that passive immunization to this extent had had no suppressive effect on the individual's response to the vaccine, a marked increase in the serum antibody levels having occurred in most of the subjects. In a control study, 85 non-ambulatory children in hospital were actively immunized with the same vaccine given either as above or in two injections 8 to 10 weeks apart. Increases in antibody levels similar to those occurring in the healthy children were observed. There was no difference between the effect produced by two injections and that

by three injections, nor was any significant difference observed in the responses of children aged 1 to 5 years as compared with those aged 6 to 12 years. In the 10 months following the primary vaccination there was a progressive decline in antibody titre to levels only slightly higher than those present before vaccination, but following a booster inoculation, the titre rose to levels as high as, and in some cases higher than, after the primary vaccination. *A. Ackroyd*

1387. **Antibody Titer for Seven Different Type I Strains of Poliomyelitis Virus in Children Vaccinated with the Mahoney Strain**

J. S. YOUNGNER and J. E. SALK. *American Journal of Hygiene* [*Amer. J. Hyg.*] **63**, 198–203, March, 1956. 3 figs., 5 refs.

The antibody titres against seven different strains of Type-1 poliomyelitis virus in 29 children given a single dose of trivalent vaccine containing the Mahoney strain were studied at the University of Pittsburgh. Neutralizing antibody was titrated by a tissue-culture colour test, trypsin-dispersed monkey kidney cells being used. It was found that the antibody titres were of the same order of magnitude with all 7 strains. Serum taken before vaccination from 15 subjects without demonstrable antibody for the Mahoney strain also failed to neutralize the other Type-1 strains. Moreover, no significant differences in the prevaccination antibody levels for the different virus strains were detected in serum from 14 subjects who had developed antibodies as a result of natural infection. These findings indicate immunological similarity among the Type-1 poliomyelitis virus strains studied. *A. Ackroyd*

1388. **Serologic Response of Infants and Preschool Children to Poliomyelitis Vaccine**

C. C. BROWN and D. C. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 399–403, June 2, 1956. 8 figs., 8 refs.

A study is reported from the University of Michigan Medical School and School of Public Health of the antibody response of infants and pre-school children to poliomyelitis vaccination. Four lots of trivalent vaccine from different commercial sources were used and a total of 251 children aged 2 months to 5 years were divided into five groups differing either in the vaccine given or the dosage schedule used.

Of the patients in the two groups which received three primary inoculations of 1 ml. at monthly intervals and a secondary inoculation after about 6 months, the vaccines used being from different sources, the majority responded with increased antibody titres against each of the three types of virus after the primary inoculations and a further rise after the reinforcing dose. Infants responded almost as well as the older children. In a third group, which received only two primary inoculations, the rise in titre after primary inoculation was not so great, while in the fourth group, consisting of infants 3 to 9 months old who received only one primary inoculation, there was only a slight rise in the titre of neutralizing antibodies against virus of Type 2 in a few cases and none at all in that against Types 1 and 3. However, after the secondary inoculation 6 months later, antibody against all three types, and in particular against Type 2, developed in both these groups, reaching a satisfactory level in the former. In the fifth group, which received three primary inoculations with a vaccine which was found to have lost much of its antigenicity owing to its preservation with thiomersalate, very little response followed the primary inoculations, but after a secondary inoculation with potent vaccine a good response occurred even when no demonstrable antibody had been present after the primary inoculations. The serological responses of the children in the age group tested were of essentially the same magnitude as those seen in children in older age groups.

Neutralization tests on the serum of some of the mothers and their children indicated that even when poliomyelitis antibodies are present in the mother's blood in high titre the protection afforded to the infant by passively transmitted antibodies lasts only for 3 to 4 months after birth, no antibodies being demonstrable after that time. *A. Ackroyd*

1389. **Immunological Studies of Brucellosis and the Immunization of Man against this Infection by Means of a Living Attenuated Vaccine.** (Recherches immunologiques sur la brucellose et immunisation humaine contre cette infection au moyen d'un vaccin vivant atténué)

P. ZDRODOWSKI, P. VERCHILOWA, and H. KOTLAROVA. *Revue d'immunologie et de thérapie antimicrobienne* [*Rev. Immunol. (Paris)*] **20**, 85–99, April–June, 1956.

Working at the Institute of Epidemiology and Microbiology (Academy of Medicine), Moscow, the authors have shown that in sheep, guinea-pigs, and rats infected with *Brucella melitensis* spontaneous cure takes place, so that after 3 years the organism can no longer be isolated from their organs; such spontaneous cure occurs more quickly in animals infected with attenuated strains. Also, in animals infected first with *Br. abortus* and subsequently infected with *Br. melitensis* the symptoms due to the latter organism clear up much faster than they do in healthy animals infected with *Br. melitensis* initially. Similarly, in some guinea-pigs first immunized with killed *Br. abortus* vaccine subsequent infections with *Br. melitensis* clear up more quickly than in unvaccinated guinea-pigs, but this immunity develops in only about 50% of the animals and lasts for no more than 3 to 4 months.

After considerable preliminary experiment, the authors decided to use a vaccine prepared from living, attenuated strains of *Br. abortus*, injected subcutaneously, to immunize man against infection with *Br. melitensis*. They claim that since the introduction of this vaccine the incidence of *Br. melitensis* infection among immunized farm-workers, slaughterhouse-workers, and others exposed to infected animals has been only about 10% of that among non-immunized workers.

[This paper is hardly more than a summary of some of the authors' experiments and results, together with some rather diffuse comment.] *C. L. Oakley*

Pharmacology

1390. **The Inhibition of Basal Gastric Secretion and of the Gastric Secretory Response to Histamine by 2:2-Diphenyl-4-di*iso*propylaminobutyramide Methyliodide in Man.** [In English]
A. MULLIE. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **106**, 447–456, June 1, 1956. 3 figs., 3 refs.

In this paper from the Polyclinic for Internal Medicine of the University of Ghent, the author describes an investigation into the effects on gastric secretion of one of the substituted phenylpropylamines, 2:2-diphenyl-4-di*iso*propylamidobutyramide methyliodide (designated R 79). This is a potent parasympatholytic substance, which is less toxic than atropine and has a longer action on oral administration. The dose used for oral administration was 30 mg. in tablets of 5 mg., and for intramuscular injection 5 mg. A total of 74 experiments were performed on 44 " untreated patients " [diagnoses not specified]. After a fast of at least 12 hours, and at various intervals after the administration of R 79 or placebo tablets, the gastric contents were removed and the gastric secretion then aspirated continuously by means of an electric pump for at least 2 hours.

During the 2 hours after an intramuscular injection of 5 mg. of R 79 a significant inhibition of basal gastric secretion was observed, a rapid fall occurring in both volume and free acidity. The gastric secretory response to 0·1 mg. of histamine per kg. body weight was also inhibited by 5 mg. of R 79 given intramuscularly one hour previously. The oral administration of a single dose of 30 mg. of R 79 caused a similar striking inhibition of basal gastric secretion lasting at least 12 hours. Side-effects, when present, were slight, some patients reporting blurring of the vision, dizziness, or a feeling of dryness in the mouth. *E. Forrai*

1391. **The Response to Acetylstrophanthidin**
L. A. SOLOFF, J. ZATUCHNI, and J. VELASQUEZ. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 733–742, April 19, 1956. 3 figs., 18 refs.

The authors have studied the effect on the healthy and diseased heart of acetylstrophanthidin, a synthetic ester of the cardiac aglycone strophanthidin, the use of which has been suggested as a short-acting digitalis-like compound in cases in which a non-cardiac illness has precipitated cardiac failure, as frequently occurs. No effect was observed in normal subjects following twice the dose (2·4 mg.) which would digitalize patients with a cardiac disorder. It was found that more of the drug was required to produce digitalization if cardiac failure was present, even if the patient had been previously digitalized. No patient fully digitalized with digoxin tolerated more than 0·6 mg. of acetylstrophanthidin.

The authors stress that the drug should always be given under electrocardiographic control, since toxic signs may be recognized on the electrocardiogram before clinical signs of toxicity appear. The therapeutic effect occurs within 10 minutes, but toxic effects may persist for 24 hours and there is no known antidote capable of abolishing such effects. *H. E. Holling*

1392. **Ethinyl*cyclo*hexylcarbamino Acid Ester as a Hypnotic in Paediatric Practice.** (Aethinylcyclohexylcarbaminsäureester als Hypnotikum in der Pädiatrie)
K. THIEL. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 774–776, May 18, 1956. 1 fig., 9 refs.

The author reports, from the Wedding Municipal Children's Hospital, Berlin, the results obtained with a new sedative drug, ethinyl*cyclo*hexylcarbamino acid ester (" valamin "), in the treatment of 47 infants and young children ranging in age from 4 weeks to 18 months.

This drug is considered to be effective and safe in use; it is rapid in its action and rapidly excreted, and shows no cumulative effect. Its hypnotic action lasts about 2 hours and its sedative action about 3. The dose used for infants was 200 mg. twice a day, which may be increased to four times a day for children of school age. As a premedication for children under 6 months of age 200 mg. was given by mouth together with 400 mg. per rectum. The author noted particular benefit from the drug in 2 cases of chorea. No deleterious change occurred in the blood picture and no side-effects were observed. *G. S. Crockett*

1393. **Dihydrocodeine. Further Development in Measurement of Analgesic Power and Appraisal of Psychologic Side Effects of Analgesic Agents**
J. S. GRAVENSTEIN, G. M. SMITH, R. D. SPHIRE, J. P. ISAACS, and H. K. BEECHER. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 877–885, May 10, 1956. 1 fig., 8 refs.

A comparative study of the analgesic potency and side-effects of dihydrocodeine, dihydro*iso*codeine, and morphine in patients with moderate or severe pain after operation is reported. The drugs, which were injected subcutaneously, were given only in response to the patient's request, and not more frequently than every 2 hours. Each patient received, per 70 kg. body weight, 10 mg. of morphine phosphate, or 30 mg. of dihydrocodeine, or 30 mg. of dihydro*iso*codeine, the order of administration being determined at random. The response to the drug was noted at frequent intervals, " good relief " being recorded when " pain was more than half gone " at 45 and 90 minutes after administration of the drug. The physical and psychological side-effects of these three drugs in groups of healthy male volunteers were also studied.

Dihydrocodeine in a dosage of 30 mg. per 70 kg. body weight was as potent as 10 mg. of morphine per 70 kg. body weight, the analgesia produced and the incidence of side-effects being about the same with each drug. *T. J. Thomson*

Chemotherapy

1394. **Behaviour *in vitro* of Some New Antistaphylococcal Antibiotics**

L. P. GARROD and P. M. WATERWORTH. *British Medical Journal* [*Brit. med. J.*] **2**, 61–65, July 14, 1956. 2 figs., 20 refs.

The authors have studied *in vitro* the behaviour of eight new antibiotics. Minimum inhibitory concentrations were determined on agar plates containing doubled dilutions of the antibiotic, the plates being inoculated with a 1-in-500 dilution of a 24-hour broth culture and read for bacterial growth after 24 hours at 37° C. To determine bactericidal action, broth containing 10 μg. of the antibiotic per ml. was inoculated with 0·01 ml. of a 24-hour broth culture per ml.; during incubation at 37° C. surface viable counts were made at 0, 2, 4, 8, and 24 hours. Habituation, cross-resistance, the effect of inoculum size, and the effect of the *p*H (5·5 to 8·5) were also studied.

The antibiotics tested were (1) erythromycin, (2) spiramycin, (3) " E 129 " and " Factor B ", (4) cephalosporin P_1, (5) micrococcin P, (6) albomycin, (7) novobiocin, and (8) vancomycin. Their approximate order of antistaphylococcal activity in tests with 55 strains of *Staphylococcus aureus* was as follows: bacteriostatic action—5, 1, 7, 3, 4, 8, 2, and 6; bactericidal action—8, 3, 1, 7, and 2 (4, 5, and 6 were not bactericidal under conditions of test). In tests with 12 strains each of Group-A *Streptococcus pyogenes* and *Str. pneumoniae*, erythromycin was the most active antibiotic. Albomycin was highly active against *Str. pneumoniae* but had no action on *Str. pyogenes* (or on 12 strains of *Str. viridans*). This was the only antibiotic with a substantial action on 9 species of Gram-negative bacilli. However, its minimum inhibitory concentrations in μg. per ml. were 0·25 for *Salmonella paratyphi* B and 0·12 for *Salm. typhimurium*, compared with 128 for *Salm. typhosa*.

Erythromycin and spiramycin were decidedly more active in an alkaline medium, but E 129 had a constant activity at *p*H 5·5 to 7·5 and was less active at *p*H 8.5. Vancomycin and micrococcin P were little affected by *p*H. Cephalosporin P_1 and novobiocin were less and albomycin was more active in an alkaline medium.

The same 6 strains of *Staph. aureus* were used in the habituation tests. Among the erythromycin group of antibiotics the greatest increase in resistance was to erythromycin itself, followed by spiramycin, the increases to E 129 and Factor B being decidedly smaller. The increase in resistance to E 129 and Factor B of organisms made highly resistant to erythromycin and spiramycin was only about eightfold. There was a consistently high degree of resistance to novobiocin; to vancomycin on the other hand the increase was only twofold to sixteenfold. Resistance developed very rapidly to cephalosporin P_1 and to micrococcin P. Many staphylococcal strains were initially highly resistant to albomycin; those which were not became resistant very rapidly.

Cross-resistance tests showed a relationship between erythromycin, spiramycin, and E 129; otherwise there was no relationship between the antibiotics studied, or between these antibiotics and penicillin, streptomycin, chloramphenicol, and tetracycline. *Joyce Wright*

1395. **Chemotherapeutic Studies with Laboratory Infections of *Schistosoma mansoni***

J. HILL. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **50**, 39–48, March, 1956.

A detailed description is given of methods employed in the routine examination of certain compounds for schistosomicidal activity. A technique is also described for the maintenance of strains of *Schistosoma mansoni* in laboratory animals which differs from the standard techniques in current use mainly in that cercariae are injected into hamsters and the livers of these animals used for the provision of miracidia for infection of *Australorbis glabratus*. For routine testing compounds were usually given orally once daily for 4 days to infected mice, the dose being one-third to one-quarter of the LD_{50}. The mice were killed 5 to 7 days after the completion of treatment and the mesenteric and portal veins (but not the liver) examined for schistosomes. Absence of worms in the portal and mesenteric veins was considered to warrant further examination of the compound concerned in different dosages.

In a study of a series of primary amino-diphenoxyalkanes with chains of 1 to 10 carbon atoms all but the methane, ethane, and decane members showed marked activity, the peak of activity occurring between the hexane and octane members, which proved much more highly active than miracil D or [trivalent] sodium antimony tartrate. " M and B 968A " (the pentane member) was given orally to 4 infected monkeys in doses of 0·1 or 0·2 mg. per g. body weight daily for 4 days. Since no diminution in ova output ensued, the two animals on lower dosage were given 0·5 mg. per g. parenterally twice daily for 4½ days. At necropsy it was considered that in one animal some drift of worms to the liver had occurred. In the other animal only degenerate ova were found in the faeces 6 days after treatment, but relapse occurred after 4 weeks. The compound exerted a temporarily deleterious effect on vision. *O. D. Standen*

1396. **Cycloserine: Antituberculous Activity *in vitro* and in the Experimental Animal**

W. STEENKEN and E. WOLINSKY. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 539–546, April, 1956. 16 refs.

In a study carried out at the Trudeau Foundation, New York, the tuberculostatic and tuberculocidal activity of the new antibiotic cycloserine was determined in liquid media, using several mycobacterial strains including *Mycobacterium tuberculosis* H37Rv. Tests were also made *in vivo* in mice which were infected

intravenously with strain H37Rv, the antibiotic being administered subcutaneously in doses of 40 to 200 mg. per kg. body weight per day for 32 days; and in guinea-pigs infected with the same strain by the intracardiac route, the antibiotic in this case being injected intramuscularly one week after infection in a daily dosage varying from 10 to 100 mg. in different treatment groups for a maximum of 55 days.

Cycloserine inhibited the growth of human virulent tubercle bacilli *in vitro* in concentrations of 6 μg. per ml. in liquid medium and of 20 μg. per ml. on solid medium. Strains of tubercule bacillus resistant to streptomycin or isoniazid showed no difference in susceptibility to cycloserine. The presence of horse serum caused a fourfold decrease in sensitivity to the drug. The greatest activity occurred at a *p*H between 6·4 and 7. *In vivo*, however, cycloserine had no significant beneficial effect on experimental tuberculosis in mice or guinea-pigs, although in the latter a blood concentration of the drug was obtained which was many times greater than the minimum concentration required for inhibition of the growth of the bacilli *in vitro*. The authors mention that in contrast to the poor results in mice and guinea-pigs, unpublished studies have shown that cycloserine has a definite but limited beneficial effect on experimental tuberculosis in rabbits and monkeys. *R. Wien*

1397. **The Relationship between the Catalase Activity, Hydrogen Peroxide Sensitivity, and Isoniazid Resistance of Mycobacteria**

R. KNOX, P. M. MEADOW, and A. R. H. WORSSAM. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 73, 726–734, May, 1956. 2 figs., 16 refs.

There is evidence to suggest that the inhibitory effect of isoniazid on the growth of *Mycobacterium tuberculosis in vitro* is due in some way to the " severe restriction of porphyrin-containing enzymes ", and it has been shown by Middlebrook that colonies of isoniazid-resistant strains of *Myco. tuberculosis* H37Rv growing on solid medium are unable to break down hydrogen peroxide, suggesting that they possess reduced catalase activity. There is, however, no one significant concentration of isoniazid at which different cultures of tubercle bacilli from patients become catalase-inactive. Thus it would seem probable that if the action of isoniazid involves inhibition either of the synthesis of catalase or of the activity of the formed enzyme, cells which are deficient in catalase might be expected to show greater susceptibility to hydrogen peroxide. The present authors, in the course of bacteriological investigations carried out at Guy's Hospital Medical School, London, on patients suffering from chronic fibro-caseous pulmonary tuberculosis, experienced difficulty in obtaining cultures of *Myco. tuberculosis* from sputum in which, nevertheless, these organisms were shown to be present by Ziehl–Neelsen staining. Such sputum usually came from patients who were receiving isoniazid in combination with either streptomycin or PAS. The authors suggest that this discrepancy could be explained by the emergence of isoniazid-resistant strains, especially as the sputum specimens had been concentrated by the method of Jungmann and Gruschka, which involves the use of hydrogen peroxide. Thus, if isoniazid-resistant cells were especially susceptible to the killing action of hydrogen peroxide they might fail to survive in sufficient numbers to yield a positive culture.

They therefore devised experiments in which the effect of isoniazid on the decomposition of hydrogen peroxide from non-bacterial sources was measured in a Warburg apparatus. These showed that the drug did not inhibit the catalase activity of blood, haemin, or a crystalline catalase preparation or the catalase activity of an isoniazid-sensitive strain of B.C.G. or of *Staphylococcus aureus*. These results suggest that it is the synthesis of the enzyme rather than its activity which is affected by isoniazid. No information could be obtained about the level of drug resistance at which catalase activity is lost, but it was shown that this loss of catalase activity in isoniazid-resistant strains is associated with an increase in susceptibility to hydrogen peroxide. On exposure to hydrogen peroxide all isoniazid-resistant cells were killed after 5 minutes, whereas isoniazid-sensitive strains were not. The authors point out that this observation is of particular importance, because in Jungmann's method of sputum concentration the sputum is treated with 0·75% hydrogen peroxide for 30 minutes and it is very likely that all isoniazid-resistant colonies will be killed and only isoniazid-susceptible colonies will grow, thus giving erroneous information about the types of organism originally present in the sputum.

[For details of the authors' experimental work the original article must be consulted.] *Kenneth Marsh*

1398. **The Action of the *para*-Aminosalicylic Salt of Isoniazid in Pulmonary Tuberculosis.** (Sur l'action du sel paraminosalicylique de l'isoniazide dans la tuberculose pulmonaire)

R. KOURILSKY, S. KOURILSKY, and Y. THUILLIER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] 32, 1948–1955, June 6, 1956. 1 fig., 20 refs.

The authors review the experimental findings reported so far of the use of the *para*-aminosalicylic (PAS) salt of isoniazid in the treatment of pulmonary tuberculosis. The argument is advanced that this compound possesses special properties which cannot be attributed merely to its isoniazid or PAS content. It has been shown to display greater activity *in vitro* than either of the parent substances against both sensitive and resistant strains of virulent tubercle bacilli. Resistance apparently also develops more slowly *in vitro* to the new compound than to isoniazid. Clinical evidence is confined to two reports, one by Smith and Wiederkehr (*Praxis*, 1953, 42, 884) and the other by Clegg at the Brompton Hospital, London (*Brit. med. J.*, 1955, 2, 1004). In the latter study, an intentionally limited pilot trial confined to 17 cases, Clegg found that the most striking change after treatment with this additive compound of PAS and isoniazid (then known as GEWO 339) was the lowering of the bacillary content of the sputum in patients suffering from chronic bilateral pulmonary tuberculosis with cavitation. The drug was well tolerated, causing much

less nausea than PAS. In only one of the 17 cases did partial resistance develop, while 2 cases in which there was partial resistance initially responded well to this treatment.

In preliminary studies carried out by the authors at the Hôpital Saint-Antoine, Paris, determination of blood concentration curves showed that the concentration of the drug persisted in the blood for a longer time than did that of isoniazid. They suggest that this persistence of the blood concentration is due to the ability of the substance to prevent the acetylation of isoniazid in the body.

[It appears very desirable that more extended trials with the PAS salt of isoniazid should be conducted in order to confirm or refute the claims that it has special properties.] *R. Wien*

1399. **The Clinical Application of Ethyleniminobenzoquinone in the Treatment of Tumours.** (Die klinische Anwendung von Äthylenimino-Chinonen bei Tumorkranken)
H. J. Wolf and N. Gerlich. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 806–811, May 25, 1956. 2 figs., 41 refs.

In view of the successful results reported by Domagk *et al.* (*Z. Krebsforsch*, 1954, **59**, 617) with the oral and local use of ethyleniminobenzoquinone in causing regression of tumours in animals, the present authors have carried out a clinical trial of this substance on patients with malignant tumours at the Municipal Hospital, Bielefeld, Germany.

The alkoxy derivative of ethyleniminobenzoquinone ("E39") was given to a patient with inoperable gastric carcinoma in doses of 5 to 10 mg. daily by mouth for several weeks, but without any effect clinically. A similar lack of response was noted in other patients treated in the same way. The daily application of a 10% suspension of E39 in "debenal" to a rectal carcinoma did not cause improvement or histological regression. E39 is practically insoluble in water, but the authors succeeded in producing a water-miscible alcoholic glycol solution suitable for intravenous, intrapleural, and intraperitoneal use and for direct injection into large tumours. The daily intravenous administration of this solution caused a depression of myeloid tissue in 2 or 3 weeks, often resulting in a leucopenia of considerable severity. Leucopenia was always produced by effective doses and the authors regard this as a sign that cytostatic concentrations were being used. Out of 72 cases of carcinoma treated with E39 leucopenia occurred in 71. Extreme leucopenia can be avoided if daily blood counts are performed and the dose adjusted accordingly. Thus with initial counts of 6,000 to 8,000 leucocytes per c.mm., treatment should be stopped when the count reaches 3,000 to 4,000 leucocytes per c.mm., or when a total dose of 700 to 800 mg. has been given. The use of other drugs causing leucopenia or of deep *x*-ray therapy concurrently with E39 is not advised. Erythropoiesis and thrombocytopoiesis were unaffected by the intravenous or intratumoral injection of E39, and haemolytic effects were never seen. Venous damage and thrombosis were avoided by careful, slow injection of the alcoholic glycol solution well diluted in water or saline.

The usual method of treatment was to begin with a daily intravenous dose of 5 mg., rising quickly to 10, 20, 30, and 40 mg., the total course never exceeding 800 mg. A deleterious effect on the appetite could be avoided by giving the injection in the afternoon. A palliative retardation of growth was achieved with intravenous therapy, particularly in those patients having multiple small metastases, and E39 was also of some value in treating residual metastases following radical surgery. Occasionally intrapleural administration of 20 to 40 mg. of E39 in 100 ml. of saline was combined with intravenous infusion in cases of exudative malignant invasion of the pleura, but local administration was liable to be followed by further chronic exudation. The over-all results in these 72 cases of tumour were: 35 improved, 14 unchanged, and 23 worse. *Norval Taylor*

1400. ***In vitro* and Clinical Effects of Urethane plus Triethylene Melamine on Human Breast Cancer**
M. M. Black and F. D. Speer. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 420–426, April, 1956. 6 figs., 8 refs.

From New York Medical College a study is reported of the effect of urethane and triethylene melamine (TEM), singly and in combination, on the dehydrogenase activity *in vitro* of tissue from 94 cases of breast carcinoma. There was a synergistic action between the two drugs in producing inhibition of the metabolic activity, but the tissue response was variable over a wide range. Clinically, urethane and TEM were given in 21 cases of breast cancer, including 7 of those in which tissue had been studied *in vitro*. In some cases there was striking clinical improvement and this appeared to be related to, and predictable from, the effects of those drugs *in vitro*.
G. Calcutt

1401. **The Influence of Hormone Therapy on Metastatic Mammary Carcinoma**
M. V. Peters. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 545–552, May, 1956. 8 refs.

Since 1940 a total of 330 patients with metastatic mammary carcinoma have received hormone therapy at the General Hospital, Toronto, and the results of this treatment are analysed in the present paper. The author's main conclusions are as follows. Hormone therapy appreciably prolonged the survival time of these patients compared with that of patients with untreated carcinoma of the breast. The best response was obtained in previously untreated cases, and oestrogen was more effective than androgen. In the older age groups the response to testosterone therapy was as satisfactory as the response to oestrogen. Administration of the last-named hormone was a more effective palliative measure in the presence of lung metastases than administration of androgen.

[The original paper should be consulted for details of the results obtained in differing cases and with varying treatment regimens.] *G. Calcutt*

Infectious Diseases

1402. **The Treatment of Typhoid Fever with Cortisone and Chloramphenicol.** (Die Behandlung des Typhus abdominalis mit Cortison und Chloromycetin)
K. CHOREMIS, T. ATHANASIADIS, C. WONTA, D. ZOUMBOULAKIS, and K. KIOSOGLOU. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **152**, 250–256, 1956. 8 refs.

At the University Paediatric Clinic, Athens, chloramphenicol in a dose of 20 to 30 mg. per kg. body weight daily combined with cortisone (75 to 100 mg. on the 1st and 2nd days and 50 to 75 mg. daily for a further 7 to 10 days) gave better results in the treatment of a trial series of 100 cases of typhoid fever in children (Group A) than did chloramphenicol alone in the same dosage given to a comparable series (Group B). In Group A 97% became afebrile in 2 to 5 days, there were no deaths, no complications, and 7 cases relapsed; in Group B the corresponding figures were 7 to 15 days, 2 deaths, 2 cases of complications, and 14 of relapse.

R. Crawford

1403. **Rubella in a Remote Community**
F. K. M. HILLENBRAND. *Lancet* [*Lancet*] **2**, 64–66, July 14, 1956. 1 fig., 16 refs.

An epidemic of rubella in Port Stanley, Falkland Islands, which began in September, 1952, and continued into the first months of 1953 is described. There had been epidemics of this disease in the Falkland Islands in 1911–12 and again in 1947–8, and some of the patients in the latter outbreak developed rubella in 1952–3. Of 1,135 inhabitants of Port Stanley, 144 had rubella, an attack rate of 12·6%. In most instances the illness was mild, and in many the infection was subclinical. Rheumatic manifestations were common, and in several cases relapsing infections were observed. In the majority of cases the lymph nodes were enlarged and continued so for as long as 7 months or even a year. A number of congenital defects were observed in infants born of mothers who became pregnant during the epidemic. The author points out that this was true of the earlier epidemics of rubella, but that the only evidence of damage to the offspring in three previous epidemics of measles and one epidemic of mumps was a single miscarriage.

G. C. R. Morris

1404. **The Blood Picture in Rubella. Its Place in Diagnosis**
F. K. M. HILLENBRAND. *Lancet* [*Lancet*] **2**, 66–68, July 14, 1956. 16 refs.

The value of changes in the blood count in the diagnosis of rubella is discussed on the basis of the differential leucocyte count in patients with clinical or subclinical infection, the patients being seen in the Falkland Islands in the epidemic of 1952–3 and in a London hospital. Initial neutropenia and lymphopenia were observed in fewer than half the cases. There was an increase in the number of monocytes. Türk or plasma cells, or both, were nearly always present, and degenerate lymphocytes were often seen. The differential count was compared with that obtained in measles, scarlet fever, and infectious mononucleosis. The author concludes that in the presence of lymph-node enlargement the differential leucocyte count is sufficiently characteristic to permit an early or retrospective diagnosis of rubella.

G. C. R. Morris

1405. **Clinical Variations in the Diagnosis of Psittacosis**
R. H. SEIBERT, W. S. JORDAN, and J. H. DINGLE. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 925–930, May 17, 1956. 4 figs., 17 refs.

Clinical variations observed in 13 cases of psittacosis and the problems of diagnosis are discussed in this paper from the Western Reserve University School of Medicine and the University Hospitals, Cleveland, Ohio. Infection with psittacosis virus may cause severe and sometimes fatal disease, or it may result only in a mild or subclinical illness. Of the 13 patients, aged 25 to 67 years, 9 were white and 4 were negroes. The illness was severe in 4, moderately severe in 8, and extremely mild in one. The findings on physical examination of the chest varied from normal to signs of marked consolidation. Other abnormal findings were delirium and stupor in one patient and hepatosplenomegaly in 2 patients; one of the latter also had acute thyroiditis and exudative tonsillitis. Leucopenia and leucocytosis were each present in 3 cases while in one case there was a raised cold-haemagglutinin titre. Radiographs revealed pulmonary involvement varying from increased bronchovascular markings to widespread infiltration throughout both lungs.

In the differential diagnosis the syndrome most frequently considered was primary atypical pneumonia; others were bacterial pneumonia, influenza, acute bronchitis, meningitis, encephalitis, typhoid fever, brucellosis, infective hepatitis, infectious mononucleosis, subacute bacterial endocarditis, rheumatic fever, carcinoma of the lung, and sarcoidosis. Specimens of serum from 11 patients were examined for the presence of antibodies to the psittacosis–lymphogranuloma group of viruses, a complement-fixation test with purified "lygranum" antigen being used. A fourfold or greater rise in titre was observed in all 11 cases, an eightfold or greater increase occurring in 10 of these. The authors consider that with the increasing popularity of parakeets a diagnosis of psittacosis must be considered in all instances of obscure febrile illness, "especially if there is a history of exposure to psittacine birds and radiographs of the chest reveal pulmonary infiltration". In all suspected cases of psittacosis, complement-fixation tests should be carried out in the acute and convalescent phases.

R. G. Meyer

1406. **Palatine Petechiae, an Early Sign in Infectious Mononucleosis**
C. B. SHIVER, P. BERG, and E. P. FRENKEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 161, 592–594, June 16, 1956. 1 fig., 17 refs.

The authors describe a petechial eruption which was seen in 21 of 38 proven cases of infectious mononucleosis. The eruption consisted of multiple pin-point petechiae on the soft palate usually near the junction with the hard palate; occasionally they were seen on the hard palate alone. In none of the cases were there any associated lesions on the skin or oral mucosa. The lesions, which varied in number from 10 to several hundreds, were noted from 3 days to 2 weeks after the onset of symptoms, lasted 3 to 11 days, and then faded without trace. Only one patient had an associated maculopapular skin eruption. In 2 cases in which the platelet count was determined and clot retraction and capillary fragility tests were performed there was no sign of a haemorrhagic diathesis.

The authors note that petechial haemorrhages in cases of infectious mononucleosis have already been described by Holzel (*Lancet*, 1954, **2**, 1054).

[It is doubtful whether any sign can be said to be specific for a disease so protean in character as infectious mononucleosis.] *I. M. Librach*

1407. **The Clinical and Epidemiological Value of the Complement-fixation Reaction for Poliomyelitis.** (Zur Frage der klinischen und epidemiologischen Bewertung der Poliomyelitis-Komplementbindungsreaktion)
W. KELLER and O. VIVELL. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **153**, 80–91, 1956. 2 figs., 16 refs.

Since complement-fixing antibodies develop early in acute poliomyelitis and persist for only a short time—whereas neutralizing antibodies may persist for years—complement-fixation tests (especially such tests as are described here, for which very little serum is required) are of diagnostic value only in the early stages of the disease. In many patients the rise in titre is specific, and the responsible virus type can be confidently diagnosed. In many others, however, unexplained heterospecific antibodies appear; although in these cases the greatest rise in titre during the infection may be suggestive of the type of infecting virus, this cannot always be safely deduced. Also, some patients never show any rise in the level of complement-fixing antibodies during infection.

In this communication from the University of Freiburg im Breisgau evidence is presented to show that poliomyelitis is extremely infectious, but that in many cases the infection is completely "silent". An account is given of the incidence of poliomyelitis complement-fixing antibodies in subjects of different ages in three widely separated areas, namely, West Africa, Charleston (South Carolina), and southern Germany. In West Africa the level begins to rise steeply at the age of 4 to 6 months, reaching its peak about the age of 4 years, whereas in the other two areas the rise is gradual, the peak not being reached until between the ages of 12 and 16 years; the striking difference between these findings is attributed mainly to the very different standards of hygiene in the areas considered. The authors suggest that infection with poliomyelitis can be regarded as having been practically universal in children of a particular age group if these subjects, when tested as adults, show no complement-fixing antibody—as is the case, for example, in persons now aged about 50 in south-west Germany in regard to poliomyelitis virus Type 2.
C. L. Oakley

1408. **Liver Function and Morphology in "Q" Fever**
B. GERSTL, E. R. MOVITT, and J. R. SKAHEN. *Gastroenterology* [*Gastroenterology*] **30**, 813–819, May, 1956. 7 figs., 17 refs.

From the Veterans Administration Hospital, Oakland, California, the authors report 6 cases of serologically proven Q fever in which the possibility of hepatic involvement was particularly investigated. Liver function tests gave inconclusive results apart from positive flocculation reactions in 5 out of the 6 cases. Biopsy was performed in 4 instances, at intervals varying from 6 days to 2 months from the onset of symptoms, and are reported as showing focal hepato-cellular damage and infiltration with monocytes and eosinophil granulocytes.

It is tentatively concluded that the liver is frequently affected in Q fever and that this diagnosis should be considered in cases of pyrexia of uncertain origin which present with clinical evidence of liver involvement.
John Fry

1409. **Visceral Larva Migrans. Report of the Syndrome in Three Siblings**
D. C. HEINER and S. V. KEVY. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 629–636, April 5, 1956. 9 figs., 16 refs.

With reference to 3 probable cases of visceral larva migrans seen recently in siblings at the Children's Medical Center, Boston, the authors review the wide variety of manifestations of this syndrome, which is caused by the ingestion of embryonated ova of roundworms infesting the dog or cat (*Toxocara canis* or *T. mystax*). The most consistent findings have been leucocytosis (12,000 to 100,000 per c.mm.) with marked eosinophilia (15 to 80%), more or less constant hepatomegaly, splenomegaly, and pulmonary infiltration leading to respiratory distress. Rashes of various kinds have been observed and the presence of larvae in the brain (causing convulsions), eyes, and other organs has been reported. Aids to diagnosis may be the presence of hyperglobulinaemia, chiefly due to an increase in the gamma-globulin fraction, and the isolation of embryonated ova of *Toxocara* spp. in soil from the garden or in the faeces of domestic pets in the patient's home. The syndrome is most commonly seen in children between the ages of one and 4 years since it is often associated with pica, which occurs chiefly in this age group. It may occur in older persons, however, through the accidental ingestion of *Toxocara* ova. It has been stated that as few as 200 ova can produce a mild form of the disease, manifested by marked eosinophilia. The present authors describe the investigations made in a family of 4 children, 3 of whom had clinical

symptoms thought to represent visceral larva migrans. Full details of the case histories are given. Treatment is mainly symptomatic; prevention of the disease by removal of the source of contamination is the most important measure. *O. D. Standen*

1410. **Serious Forms of Digestive and Hepatic Ascariasis in Children.** (Les formes médicales graves de l'ascaridiose digestive et hépatique chez les enfants)
N. NEIMANN, M. PIERSON, and G. DEBRY. *Pédiatrie* [*Pédiatrie*] **11**, 317–333, 1956. 3 figs., bibliography.

As a result of their experience at the University Children's Clinic, Nancy, during the past 12 years the authors draw attention to the occasional seriousness of the manifestations of intestinal and hepatic ascariasis and distinguish, with illustrative case histories, five important syndromes. (1) That described as the *syndrome ascaridien* includes fever, loss of weight, digestive troubles, affections of the skin, mucous membranes and lungs, visceral haemorrhages, haematological changes, and abnormal radiological appearances, which are due to absorption and retention of barium by the parasites. (2) The " abdominal syndrome " is manifested by signs and symptoms which most closely resemble those of appendicitis, the most characteristic being gastric flatus, borborygmi, and occasionally the presence of a group of worms demonstrable by palpitation. (3) A " typhoidal form " is illustrated by one case only [but the syndrome as described is not convincing]; in this type gastrointestinal dyspepsia leading to refusal of food may result in serious malnutrition if the condition is prolonged. (4) The " toxic syndrome " is manifested by anorexia, vomiting of increasing intensity, and finally a febrile gastro-enteritis with mucoid or liquid stools, which may lead to a clinical picture of neurotoxaemia. (5) " Hepatic ascariasis ", in which there is enlargement of the liver, sometimes with abscess or granuloma.

In the absence of ova in the stools, as in all-male infections, ascariasis is best diagnosed by radiology. The paper concludes with a review of the anthelminthic substances which have been employed in the treatment of ascariasis. *O. D. Standen*

1411. **Treatment of Enterobiasis and Ascariasis with Piperazine**
H. W. BROWN, K. F. CHAN, and K. L. HUSSEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 515–520, June 9, 1956. 18 refs.

The authors review the reported results obtained with piperazine in the treatment of enterobiasis and ascariasis and describe, in this paper from Columbia University, New York, a trial in which a high dosage was given over short periods. Piperazine citrate syrup was given once daily for 7 days to 60 patients with enterobiasis, the dosage of the drug being 1 or 2 g. a day, according to weight, expressed in terms of piperazine hexahydrate. The syrup was taken 30 minutes to one hour before breakfast, followed by a glass of water. At the end of treatment anal swabs were examined daily for the presence of eggs, a negative swab on 7 consecutive days indicating cure. Of the 60 patients, 58 were cured. The authors state that several salts of piperazine have been found to be effective; of 74 patients given piperazine phosphate, 66 were cured, while of 12 given two 7-day courses of calcium dipiperazine dicitrate, 10 were cured.

In cases of ascariasis piperazine citrate syrup was given 1½ to 3 hours after breakfast on one day or on 2 consecutive days, the daily dose being equivalent to 3·5 g. of piperazine hexahydrate. With the one-day treatment 34 out of 46 patients were cured and the total egg count was reduced by 92%; with the 2-day treatment 50 out of 53 patients were cured, the total egg count being reduced by 99·6%. Administration of a single dose of the drug before breakfast achieved a cure in 15 out of 21 patients and a total egg reduction of 95%. From this it is concluded that the presence of food in the gut has little, if any, effect upon the activity of piperazine against *Ascaris*.

Further tests showed that piperazine was of little or no value against *Necator americanus*, *Trichuris trichiura*, *Strongyloides stercoralis*, *Hymenolepis nana*, or *Giardia lamblia*. Piperazine citrate was well tolerated when given in the recommended dosage, but the authors point out that overdosage may cause neurological side-effects and that in patients suffering from nephritis the standard dosage of the drug may cause mild nausea, vomiting, or urticaria. *O. D. Standen*

1412. **Treatment of Enterobiasis with One Oral Dose of Promethazine Hydrochloride**
J. L. AVERY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 681–683, June 23, 1956. 15 refs.

The literature on the incidence, pathology, and symptoms of enterobiasis is reviewed, and the many drugs which have been tried in treatment are discussed. Some of these, including piperazine and gentian violet, are dismissed as unsatisfactory " for one or more reasons, mainly insufficiency of action, toxicity, inconvenience, and expense ".

In view of recent claims of the successful treatment of enterobiasis in Egypt with promethazine, the author tried this drug in 100 cases of threadworm infection, 125 mg. being given in a single dose at bedtime, without preliminary fasting. Ten days later one or more anal swabs were taken and examined. It is claimed that 97% of the patients were rendered free from infection, as shown by " continuous negative post-treatment anal swabs ". [Apart from the reference to one or more swabs being taken, no details of the number or frequency of post-treatment examination are given.] Anal swabs from a number of patients showed evidence of re-infection 53 days to several months after treatment was completed.

No untoward side-effects were encountered, although nightmares were reported in a few patients aged 4 to 8. In one instance nightmares recurred when treatment was repeated for re-infection some months later. To overcome sleep disturbances it is recommended that a hypnotic be given on the night following treatment.
O. D. Standen

Tuberculosis

1413. **The Results of Vaccination with B.C.G. in the Town of Montreuil, 1948–55.** (Résultats de la vaccination B.C.G. dans la ville de Montreuil de 1948 à 1955)
M. Fourestier, A. Blacque-Belair, J. J. Chamouard, A. Gladu, and J. Marsault. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd.* (*Paris*)] **140**, 274–282, May 15, 1956. 3 figs., 5 refs.

Between 1948 and 1955 over 9,000 tuberculin-negative individuals living in the town of Montreuil were vaccinated with B.C.G. vaccine. This constituted 12% of the total population and almost 40% of the population aged 19 years and under. This record is compared with that of another town of comparable size in which only 2,132 vaccinations have been performed, the first in 1953, representing 8% of the population up to the age of 19.

Before vaccination was begun in Montreuil the incidence of tuberculosis in persons up to the age of 19 was three times higher than in the control town (403 as against 155 per 100,000). Seven years later the situation was reversed, the rates being 65 per 100,000 for Montreuil and 169 per 100,000 for the control town. This change was most evident in the age group 5–14 years.

The vaccination programme in Montreuil has not so far affected mortality from tuberculosis compared with the control town, since deaths from tuberculosis occur mainly in the older age groups not affected by vaccination. Moreover, it has not so far had any influence on the incidence of forms of tuberculosis other than primary lesions. *T. M. Pollock*

1414. **Vole Bacillus Vaccine: Tuberculin Sensitivity in African Children after Small Doses**
C. L. Greening. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 93–97, April, 1956. 12 refs.

An investigation to determine the minimum dose of vole bacillus vaccine producing tuberculin allergy in African children aged 7 to 17 years is reported from Ndola, Northern Rhodesia. Tests for tuberculin sensitivity were carried out, the Heaf multiple-puncture technique with a dose of P.P.D. equivalent to 10 t.u. being used. The reactions were read after 7 days, and all tuberculin-negative subjects were vaccinated. Vaccination was by multiple puncture with a Heaf apparatus set to 2 mm., and the concentrations of the vaccine were 0·5, 0·25, 0·125, 0·062, 0·031, 0·016, 0·008, and 0·004 mg. per ml. of vole bacillus culture. Care was taken to guard against the effect of strong light during vaccination. After an interval of 8 weeks the vaccinated children were subjected to tuberculin sensitivity tests.

A total of 440 children were vaccinated and tuberculin tested. With the highest concentration of vaccine the conversion rate was only 42%, while with the lowest concentration it was 20%. Of 103 children who gave a negative reaction 9 weeks after vaccination, 60 gave a positive reaction at 29 weeks. *T. M. Pollock*

1415. **Mantoux and Heaf Multiple Puncture Tuberculin Tests: Comparison in BCG Vaccinated and Unvaccinated Subjects**
E. Low. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 102–110, April, 1956. 2 figs., 11 refs.

In an investigation at Fort Qu'Appelle Sanatorium, Saskatchewan, Canada, a comparison was made between the Mantoux test and the Heaf test in 420 B.C.G.-vaccinated and 620 unvaccinated subjects. Each individual was given a Mantoux test with 10 t.u. old tuberculin on one forearm and a multiple-puncture test on the other, for the latter the Heaf multiple-puncture apparatus and adrenalinized undiluted old tuberculin being used. The reactions were noted at 48 hours. The Heaf test was found to be more sensitive than the Mantoux test in both groups, giving 15% more positive reactions in the vaccinated subjects and 7% more in the unvaccinated. The Heaf reactions were easier to read than the Mantoux reactions; also there were fewer intense reactions with the Heaf test. The time spent in preparing the equipment required was much less with the Heaf test than with the Mantoux test. In consequence it is concluded that the Heaf test is superior to the Mantoux test for tuberculin survey work. *T. M. Pollock*

1416. **Mantoux Reaction Patterns in Active and Arrested Tuberculosis**
F. O'Grady. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 159–169, April, 1956. 4 figs., 11 refs.

The author, working at the Connaught Hospital (Army Chest Centre), Hindhead, Surrey, has observed that there is sometimes a difference in type between the Mantoux reaction elicited in patients with active tuberculosis and that produced in healed cases. In this paper he compares the results recorded in 56 Mantoux-positive young Servicemen in whom active disease had been excluded (and who had not been tuberculin-tested within the preceding 3 months) with those obtained in 54 cases of active tuberculosis and 22 cases of pleural effusion. For the initial test 0·1 ml. of old tuberculin in a dilution of 1 in 10,000 was injected intradermally, and repeated if necessary with 0·1 ml. of 1 in 1,000 or 1 in 100; the author does not consider that variation of dosage required to produce a reaction materially affected the subsequent observations. An area of easily palpable induration 6 mm. in diameter after 48 hours was regarded as a positive reaction.

In the subjects not suffering from active tuberculosis three kinds of reaction were observed. (1) In the commonest type of response—details of criteria for erythema, and for area and depth of induration are given—the reaction was greatest on the second or third day and remained plainly detectable for 6 to 15 days. (2) The second type of response was characterized by marked symmetry of dimension and reached its maximum on the

fourth or fifth day. (3) The third and rarest reaction became well developed in 24 hours and in no case reached its maximum after 48 hours. In many of the cases of active tuberculosis the reactions were similar to the above, but in more than half (51·8%) they were characterized by extreme transience and by "shallowness" of the induration. In 7 (31·8%) of the cases of pleural effusion similar reactions were observed. This type of reaction has not so far been encountered in any patient not suffering from active tuberculosis. The author suggests that such modifications of the normal reaction may be due to a form of autogenous desensitization occurring in response to an antigen. He stresses, however, that it cannot be assumed that the changes in the skin reaction are paralleled by similar changes in the tuberculous lesions, although the possibility of such a relationship is not excluded. *R. J. Matthews*

1417. **The Effect of Sarcoidosis Sera on the Tuberculin Response.** [In English]
B. MAGNUSSON. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **36**, Suppl. 35, 1–138, 1956. 13 figs., bibliography.

RESPIRATORY TUBERCULOSIS

1418. **Factors Influencing the Attack Rate of Pulmonary Tuberculosis**
A. L. COCHRANE, T. F. JARMAN, and W. E. MIALL. *Thorax* [*Thorax*] **11**, 141–148, June, 1956. 8 figs., 18 refs.

The knowledge likely to be most useful in the prevention of a chronic disease is that of the factors influencing its attack rate. The authors, working at Llandough Hospital, near Cardiff, have therefore determined the attack rate for pulmonary tuberculosis among the population of the Rhondda Fach, a comparatively isolated Welsh coal-mining valley. This population was radiographed in 1950–1, and 95% of those still available re-examined in 1953 after a mean interval of 2·6 years. Unfortunately, the follow-up of male non-miners in the 15–19 and 19–24 age groups was incomplete (62·5 and 80·1% respectively) because many had left the valley, chiefly as a result of the military call-up.

The annual attack rate for females was 0·9 per 1,000 and for non-mining males 2·0 per 1,000. It appeared that the lesions diagnosed in elderly males were the end-results of "attacks" in early adolescence which had remained quiescent. Contact with infectious cases was a most important factor; thus the attack rate among females in the 15–24 age group with such contact was 1·5%, compared with 0·2% for non-contacts; for male non-miners the corresponding figures were 6·2 and 0·6%. As a measure of the success of the attempt which has been made to reduce the infectivity in the valley as compared with other areas where no such attempt has been made, it was shown that the attack rate among females in the 15–24 age group living in but working outside the valley was 0·5%, compared with 0·1% for those both living and working within the valley; the differences in attack rate in relation to age, sex, and occupation were hardly significant in comparison. The authors calculate that had B.C.G. vaccination been given to Mantoux-negative children aged 5 to 14 in the year 1950–1, there would have been a reduction of 15% in the attack rate, suggesting that B.C.G. vaccination "can only be an adjunct to and never a substitute for the control of infection by case finding and admission to hospital".

The survey also showed that the annual attack rate for tuberculosis among non-miners was much higher, especially in the 15–24 age group (6·8 per 1,000), than among miners with simple pneumoconiosis of Categories 0 and 1 (0·9 per 1,000). The latter rate was also much lower than that among miners aged 35 to 44 with simple pneumoconiosis of Categories 3 and 4, among whom it was 13·4 per 1,000. Exposure to coal dust thus appears to modify and postpone the attack rate.

The authors conclude that the only logical first step towards the control of tuberculous infection is to radiograph everyone. They did not find this easy, even in their small-scale attempt, and they put forward the case for compulsory radiography, believing that this small sacrifice of personal freedom would be accepted by most people once they were convinced that it would lead to the eradication of tuberculosis. *Kenneth Marsh*

1419. **The Prognosis of Bilateral Symmetrical Diffuse Nodular Pulmonary Tuberculosis and its Possible Relationship to Intestinal Tuberculosis**
R. S. MITCHELL. *Diseases of the Chest* [*Dis. Chest*] **29**, 669–674, June, 1956. 2 figs., 8 refs.

The possible relationship between the type and distribution of pulmonary tuberculous lesions and the presence of intestinal tuberculosis was studied in the follow-up records of 1,504 patients admitted to the Trudeau Sanatorium, New York, between 1930 and 1939 with active advanced pulmonary disease. In 1,429 cases the 5-year results were available for analysis. The author states that a barium-meal examination was carried out as a routine in all cases on admission.

In 44 of the 1,429 cases bilateral diffuse nodular shadows were seen on the radiograph, and in 19 (43·2%) of these intestinal tuberculosis was present. Of the 1,385 cases with the more usual radiological appearances, 99 (7·2%) had intestinal tuberculosis. Thus of 118 patients with intestinal tuberculosis, 19 had diffuse nodular shadows, compared with 25 out of 1,311 without intestinal tuberculosis.

The 5-year results were not significantly worse in tuberculous patients with intestinal tuberculosis than in those without. However, the prognosis in patients with diffuse nodular pulmonary tuberculosis was not so good as that in patients with other forms of the disease. A study of the findings over a 20-year period revealed increased morbidity and mortality in patients with diffuse nodular tuberculosis.

It is suggested that these bilateral nodular shadows are a manifestation of haematogenous spread from a small-bowel focus via the thoracic duct and inferior vena cava to the lungs. *Denis Abelson*

1420. **The Treatment of Tuberculosis in Man with Cycloserine.** (Traitement de la tuberculose humaine par la cyclosérine)

A. RAVINA and M. PESTEL. *Presse médicale* [*Presse méd.*] **64**, 1241–1245, July 4, 1956. 6 figs., 16 refs.

The authors describe, from the Hôpital Beaujon, Paris, the results of the treatment with cycloserine of 80 patients with pulmonary tuberculosis. The drug was given orally in doses of 250 mg. daily, which was increased gradually to 1 or 1·5 g. daily, the total period of treatment lasting 6 months or more; some of the patients were given isoniazid in addition. There were toxic cerebral reactions in 12 cases, ranging from neurotic manifestations to convulsions. The series included cases of chronic cavitary lesions, most of them resistant to orthodox chemotherapy, cases of recent infiltration, and also a few cases of pleurisy and disseminated forms of tuberculosis [but the numbers of each type are not given]. In most cases, even those with old cavities, the clinical, bacteriological, and radiological response was good. [Many convincing case histories are given, but there is no detailed analysis of these results.] In particular, fever invariably and promptly abated, weight usually increased by 4 or 5 kg. in a few weeks, cough disappeared in a few days, and the sputum diminished in quantity and in most cases became free of tubercle bacilli within 2 to 5 weeks.

In discussing the mode of action of cycloserine the authors mention [without further precise analysis] the weakness of the bacteriostatic action of cycloserine *in vitro* and the apparent enhancement of such activity *in vivo*, which may, they suggest, be the result of some change in the size of the molecule in the body. The absence of resistance to the drug, even after 6 months of treatment with it alone, is also pointed out. The authors conclude that cycloserine is a drug of great interest and promise in the treatment of pulmonary tuberculosis.

Arnold Pines

1421. **Chemotherapeutic Control in Fibronodular Pulmonary Tuberculosis**

G. TODD, D. TEARE, and W. I. GORDON. *Lancet* [*Lancet*] 2, 1–4, July 7, 1956. 2 figs., 1 ref.

The authors have attempted to correlate the pathological findings in operation specimens of lung tissue with the preoperative clinical and laboratory findings in 238 consecutive cases of pulmonary tuberculosis subjected to surgical resection at King Edward VII Sanatorium, Midhurst, Sussex, after treatment with various combinations and dosages of antibiotics. In this way they hoped to ascertain what type of combination should be used and the optimum duration of treatment before operation. Segmental resection had been performed in 178 cases, lobectomy in 58, and pneumonectomy in 2. Each resected specimen was examined shortly after removal and palpable areas of solid disease were incised for smear and culture under sterile conditions.

Of the 238 cases, 130 were symptomless and in 106 no tubercle bacilli had been detected in the sputum or by laryngeal swabbing at any time before operation. Most of the patients had been treated with streptomycin (1 g. daily for 30 days, then every other day) combined with isoniazid (200 mg. daily for 30 days, then every one or 2 days), or streptomycin (in the above dosage) with PAS (16 g. daily), but some had received all three drugs (the dosage of each being as above). Some had received continuous treatment, others two or more courses separated by intervals of 28 days or longer. No significant difference in the incidence of positive smears or cultures from the resected specimens was found between cases in which preoperative cultures had been positive and those in which they had been persistently negative, or between those given continuous and those given discontinuous chemotherapy. However, in those cases in which the total dose of streptomycin had been more than 100 g. the number of negative cultures obtained from the resected specimens was significantly higher than that of positive cultures, whereas in cases in which less than 100 g. had been given the numbers were approximately equal. No appreciable difference in postoperative progress was demonstrable between patients receiving short courses and those receiving long courses of drugs before operation, and it is concluded that no harm results in selected cases from early operation (that is, after a 9-week course). Of 155 specimens from patients who had received streptomycin and isoniazid, 61 gave positive and 94 negative cultures; of the 14 from patients treated with streptomycin and PAS, 11 gave positive and 3 negative cultures; and of the 69 from patients given all three drugs, 33 gave positive and 36 negative cultures.

From the findings in these cases the authors consider it to be impossible, even with prolonged chemotherapy, to be certain on clinical and radiological grounds alone that a lesion which appears to be quiescent will not break down. They therefore conclude that the safest way to ensure complete recovery in localized fibronodular pulmonary tuberculosis is to resect the diseased area. They recommend the continuation of chemotherapy for 12 months after operation, at least 6 months' postoperative care being given in an institution.

Norman F. Smith

1422. **Pyrazinamide–Isoniazid. Comparison with Isoniazid–*para*-Aminosalicylic Acid in Active Pulmonary Tuberculosis with the Choice of Regimens Determined by Chance**

S. PHILLIPS and G. E. HORTON. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 704–715, May, 1956. 4 figs., 17 refs.

Pyrazinamide alone, or in combination with isoniazid, is known to produce a very marked beneficial effect in pulmonary tuberculosis, but it has the disadvantage of being toxic to the liver and its routine use has generally been considered inadvisable. The present authors, however, in an attempt to decide whether or not the results which could be obtained with pyrazinamide and isoniazid were so markedly superior that it would be justifiable to " regard a certainly relatively low incidence of hepatotoxicity as tolerable ", have carried out a study at the Veterans Administration Hospital, Memphis, Tennessee, on 93 sputum-positive tuberculous patients, all male

and selected at random. Of these patients, 38 (Group 1) received pyrazinamide, 750 mg. four times daily, and 100 mg. of isoniazid thrice daily, while the remaining 55 (Group 2) were treated with PAS and isoniazid. In all the patients receiving pyrazinamide liver function tests were performed at monthly intervals and the serum bilirubin and alkaline-phosphatase levels were determined.

At the end of 4 months the proportion of patients showing substantial radiological improvement in the two groups was almost identical (55 and 58% respectively), while 82 and 87% respectively began to show negative sputum on microscopy; but more patients in Group 1 than in Group 2 had sputum which was negative on culture (82% compared with 67%). Somewhat similar results were obtained at the end of 8 months. Finally, 8 patients in Group 1 and 16 in Group 2 were treated for 12 months or longer. The proportion showing *x*-ray improvement was considerably greater in Group 1 (76% compared with 56%), but the small number of patients makes it difficult to evaluate this difference; however, the sputum-conversion rates were identical (87% in both groups).

No case of isoniazid resistance occurred in Group 1, but there was one such case at 5 months in Group 2. In the latter group, also, 4 patients developed gastro-intestinal symptoms, although 3 improved when PAS was withheld for a few days; the fourth patient, however, had to cease treatment after 12 months because of persistent diarrhoea. In Group 1, 2 out of the 38 patients developed jaundice, and therapy with pyrazinamide had to be discontinued in 3 other cases when the retention of dye in the " bromsulphalein " test was repeatedly higher than 15%. The authors [wisely] conclude that this degree of toxicity is probably too high a price to pay for the very slight therapeutic advantage afforded by pyrazinamide. *Kenneth Marsh*

1423. **Large Dose Isoniazid Regimen for Pulmonary Tuberculosis. Effect of Glutamic Acid. Management of Drug Toxicity with Pyridoxine**
I. TCHERTKOFF, S. IKARD, C. ADAMSON, and R. YILMAZ. *Sea View Hospital Bulletin* [*Sea View Hosp. Bull.*] **16**, 62–79, July, 1956. 8 figs., 11 refs.

1424. **The Surgery of Pulmonary Tuberculosis; a Twelve-year Experience**
J. L. ROBINSON, J. C. JONES, B. W. MEYER, and F. S. REDING. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 690–703, May, 1956. 4 refs.

In a highly detailed statistical review the authors assess the results of surgical treatment in 1,363 cases of pulmonary tuberculosis seen over the 12-year period 1943–54. In the early years thoracoplasty was the operation of choice, but with the advent of chemotherapy in 1946 this operation was abandoned in favour of resection. The indications for resection (458 cases) were those generally accepted. In this group the early operative mortality (within 10 days of operation) varied directly with the amount of lung resected, from 1% for segmental resection up to 7% for pneumonectomy, the over-all early mortality being 2·8%. There was a similar variation in the late mortality, the over-all figure for all resections being 5·2%. The mortality rate was higher among males than females, particularly males subjected to operation on the right lung. Generally speaking, the influence of chemotherapy was most noticeable in the reduction in late operative mortality.

Over the period under review the authors' practice as regards post-resection thoracoplasty varied. They now consider that thoracoplasty should be performed on all patients who have had a pneumonectomy, on those in whom it is apparent that the remaining lobe will not fill the chest, and on patients with any degree of pulmonary emphysema. There was very little difference between the survival rate after resection and the survival rate after thoracoplasty, but the percentage of patients who were well and who had a negative sputum was much higher among those subjected to resection than among those subjected to thoracoplasty.

[There is a close correlation between the authors' findings and those of other surgeons treating pulmonary tuberculosis.] *A. M. Macarthur*

1425. **Results of Decortication in Chronic Tuberculous Pleurisy.** (Résultats de la décortication des pleurésies tuberculeuses chroniques)
P. HERTZOG, L. TOTY, C. PERSONNE, J. CHEVASSU-PÉRIGNY, and J. L. ACCRAD. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **20**, 324–340, April, 1956 [received July, 1956]. 16 figs.

The authors state that now that tuberculous empyema seldom arises as a complication of the therapy of pulmonary tuberculosis a far more satisfactory method of treatment than any of those formerly practised is available in decortication, a one-stage operation which causes no deformity and which is applicable to nearly all cases, no matter how long-standing, when medical treatment has failed. Its aim is the complete elimination of the pleural sac and of all dead space.

In this paper they report the results in 188 patients, all with tuberculous empyema, who were treated by decortication during the period 1951–5. The ideal aim —complete excision of the unopened sac—was achieved in one-fourth of the cases, but piecemeal removal gave satisfactory results. A long incision is necessary, sufficient to give access to both apex and diaphragm. The parietal layer is freed in the extrapleural plane, with special care near the large vessels and nerves at the apex, and the visceral layer, which is always thinner, just superficial to the visceral pleura; this procedure generally presents no difficulty, except over areas of lung affected by tuberculous disease. The whole lung must be freed and haemostasis must be meticulous. Associated resection of pulmonary tissue is indicated in the presence of bronchial fistula, bronchial stenosis, cavitation, or the presence of a caseous focus; it is usually unnecessary and undesirable to resect areas affected by scarring, small nodules, or emphysema, but drainage tracks and cold abscesses are excised from the chest wall. Only catgut sutures are used, and two drainage tubes are left

in place. Great care must be taken in the first post-operative days to maintain full pulmonary expansion, confirmed by radiographic control, for as the authors state, " the case is won or lost in the first 10 to 12 days ". If pleuropneumonectomy is necessary, simultaneous resection of ribs to obliterate the remaining space reduces the risk of re-infection.

Of the 188 cases, 155 were completely successful in that the pleural sac was entirely removed and the lung expanded fully; in 106 of these cases decortication had followed intrapleural pneumothorax and in 49 extrapleural pneumothorax. It is stated that the thickness of the sac and the nature of its contents had little effect on the results, which depend chiefly on the state of the underlying lung. Poor results were more frequent in cases in which an extensive resection was necessary. There were 5 deaths in the series, one during operation.

In the 28 remaining cases decortication was not completely successful, usually because an apical pocket of empyema persisted. In 18 of these this was closed by a limited upper thoracoplasty, giving 173 satisfactory results (92%) in all. In 8 cases subsequent parietectomy was necessary, with eventual healing by scarring in 6, while in 2 cases suppuration persists.

[The principles and results here described correspond to modern practice in Great Britain.]

M. Meredith Brown

1426. **Bronchographic Studies after Resection for Pulmonary Tuberculosis**

J. E. WALLACE and R. PILLMAN. *Thorax* [*Thorax*] **11**, 149–159, June, 1956. 20 figs., 5 refs.

In an attempt to assess the anatomical changes taking place and the degree of over-expansion in the residual lung after resection for tuberculosis the authors, at Aldingbourne Sanatorium, Chichester, studied the bronchograms obtained after resection in a total of 49 cases and discuss their findings in the present paper.

In an " unassisted " upper lobectomy—that is, without a concomitant space-filling procedure—the residual space is filled by over-expansion of the apical lower segment and upward displacement of the middle lobe or lingula if these lobes are retained. The basal segments of the lower lobe remain undisturbed unless the middle lobe or lingula has been removed, in which case the anterior basal segment takes part in the over-distension and upward displacement. It is concluded that residual disease in the apical lower lobe, middle lobe, or lingula after unassisted upper lobectomy is particularly liable to stress and reactivation by over-expansion.

In lower lobectomy there is little distension of remaining lung tissue if the lingula or middle lobe is retained. These segments are displaced backwards but do not suffer over-expansion. If the upper lobe only is retained the apical segment never takes part in the space-filling, and it is concluded that residual disease in this area is not particularly at risk after lower lobectomy. If the diaphragm is raised after lower lobectomy there is very little change in the remaining upper lobe. A post-resection thoracoplasty prevents over-distension but not necessarily displacement of the anterior-lying lung tissue. On the other hand, upper-lobe resection after thoracoplasty is not followed by either displacement or over-distension. Resection of the apico-posterior segments is followed by very little change, particularly if there is a good remaining anterior segment.

Pooling of the medium in the main bronchus is constantly noted after unassisted left upper lobectomy. In all cases the displacement is upward and backward. This pooling may occur after right upper lobectomy, but never after lower lobectomy or after upper lobectomy with post-resection thoracoplasty. Pooling may occur in the stump after lower lobectomy. It is suggested that these changes may lead to sputum retention and late suppurative complications.

The authors consider that their findings lend support to the policy of carrying out post-resection thoracoplasty where there is residual disease in the apical lower segment, middle lobe, or lower lobe, and of crushing the phrenic nerve after lower lobectomy with residual disease.

A. M. Macarthur

1427. **Late Results of Resections for Tuberculosis of the Upper Lobe**

E. HOFFMAN. *Thorax* [*Thorax*] **11**, 160–162, June, 1956.

Of 112 patients subjected to resection for pulmonary tuberculosis of the upper lobe at Poole Sanatorium, Nunthorpe, and Shotley Bridge Hospital, Newcastle upon Tyne, between 1949 and 1954, 100 were followed up for one to 6 years. The findings indicate that upper lobectomy is a satisfactory procedure in cases in which thoracoplasty has failed and in those with residual caseous foci or fibrocaseous disease limited to a segment of lobe. In patients with large upper-lobe cavities and bilateral fibrocaseous disease the results of lobectomy are poor, and the author considers that in these patients five-rib thoracoplasty with adequate chemotherapy is the procedure of choice.

A. M. Macarthur

1428. **Loss of Ventilatory Function after Surgical Procedures for Pulmonary Tuberculosis**

G. M. LITTLE. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 172–176, June, 1956. 6 refs.

In a study carried out at the King George V Hospital for Diseases of the Chest, Godalming, Surrey, the ventilatory function was measured in 272 male patients with pulmonary tuberculosis before and again 3 months after various operative procedures. There is normally a good correlation between the maximum breathing capacity (M.B.C.) and the one-second timed vital capacity (T.V.C.1), but in this investigation the T.V.C.1 proved to be a more reproducible measurement than the M.B.C.

In 25 patients the induction of a pneumoperitoneum resulted in a mean loss of 8·5% in the T.V.C.1, and in 9 cases in which phrenic crush was added to pneumoperitoneum the mean loss increased to 19·1%. There was no significant difference between the decrease in the mean T.V.C.1 in 57 patients subjected to segmental resection alone (14%) and that in 16 patients undergoing lobectomy alone (16%). The loss of ventilatory function was considerably greater, however, when these procedures were accompanied by thoracoplasty, and

increased with the number of ribs involved: thus after 5-rib thoracoplasty the mean loss was 21% and after an 8-rib thoracoplasty it was 35%. The greatest loss in ventilatory function was observed in 6 patients subjected to lobectomy followed later by thoracoplasty; in these cases the mean loss for the double operation was 39·3%.

E. Keith Westlake

EXTRA-RESPIRATORY TUBERCULOSIS

1429. **Tuberculous Meningitis in Children**

G. BOYD. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 477–484, May, 1956. 14 refs.

The author reviews her experience at the Hospital for Sick Children and the I.O.D.E. Hospital for Tuberculosis, Montreal, in the treatment of tuberculous meningitis since the advent of streptomycin. Altogether, 142 bacteriologically proven cases were treated during a period of 8½ years, but as 8 of the patients died within 24 hours these are not included in the analysis of the results. In 23 cases the patient was considered to have a primary spinal-cord infection, with or without Pott's disease, from which meningeal dissemination had taken place. In the remaining 111 cases the chief adverse factors in prognosis were delay in diagnosis, age under 2 years, and the presence of large caseous masses in the chest. Since the advent of isoniazid all but the first of these factors have become less important.

Treatment has changed with increasing experience and the successive introduction of new drugs, but prolonged bed rest, the adequate control of electrolyte balance, and the relief of increased intracranial pressure are still considered to be of great importance. Intraventricular tuberculin was used, before isoniazid became available, in 25 extremely advanced cases; 10 of these patients survived, 4 being in good condition. Intrathecal treatment has been abandoned since the introduction of isoniazid, and at present streptomycin, 0·5 g., is given twice daily for 3 months and then every second or third day for another 3 months, with isoniazid by mouth, 10 mg. per kg. body weight initially, followed by 5 mg. per kg. for 3 months and finally 2·5 mg. per kg. for 3 months. Craniotomy is occasionally performed to relieve raised intracranial pressure.

Altogether 51 patients (including one who was unconscious for 7 months) were completely cured, the proportion of such cases increasing with advances in treatment. There are 11 survivors with severe mental damage (I.Q. less than 60), and 2 others show extreme behaviour disorders; 2 survivors are epileptic, though not necessarily as a result of the meningitis; and 6 otherwise normal children have mild spasticity of the legs. Deafness was very common before isoniazid treatment and 4 mentally normal and most of the defective children remain deaf, a few others having slight hearing loss. Some recovery of hearing lost as a result of streptomycin treatment is possible, however, and in one case this occurred 3½ years after the acute illness. Only 2 children remained blind after the acute illness, and in one of these vision has returned sufficiently to permit school attendance. Intracranial calcification was seen in 4 survivors. Altogether 40 patients have died [plus the 8 excluded from the series], and 51 have recovered with no sequelae, 13 with moderate sequelae (including deafness in 9 cases), and 25 with severe residual damage.

[According to the tabulated results, of 41 children treated in the 3 years 1952–4, 7 died and 4 of the survivors suffered severe residual damage, yet it is stated in the text that since the current treatment regime was adopted (in March, 1952) " there have been no deaths and no complications in 40 cases other than slight squint (3 cases) and one transitory vestibular disturbance ". This and other discrepancies between the tables of results and the text make evaluation of the paper and of the results difficult.]

John Lorber

1430. **Effects of a New Tranquilizing Drug (Nostyn) on the Behavior Patterns of Children Recovered from Tuberculous Meningitis**

C. L. ASUNG, A. I. CHARCOWA, and A. P. VILLA. *Sea View Hospital Bulletin* [*Sea View Hosp. Bull.*] **16**, 80–85, July, 1956.

1431. **Early Diagnosis of Bone and Joint Tuberculosis in Children**

T. J. MILLS, R. OWEN, and E. H. STRACH. *Lancet* [*Lancet*] **2**, 57–59, July 14, 1956. 8 refs.

The effective use of antibiotics in the treatment of bone and joint tuberculosis demands early diagnosis, and in this paper from the University and the Alder Hey Children's Hospital, Liverpool, the value of aspiration and of biopsy in the investigation of 60 consecutive cases is discussed. In 35 cases the diagnosis of tuberculosis was established by isolation of the bacillus or by the typical histological changes, while in 20 cases the biopsy was of value in excluding tuberculosis and helped materially in the diagnosis of other conditions; in 5 cases the biopsy findings were inconclusive.

The local examinations were as follows. (1) Aspiration. In the presence of joint effusion the fluid was aspirated and examined microscopically, cultured, and inoculated into guinea-pigs. False negative results were occasionally obtained, but false positive results were not observed. Aspiration of an abscess gave a false negative result in only one case. (2) Lymph-node biopsy. This was performed in cases with joint lesions and periosteal foci in bone. No false positive and only two false negative results were seen. (3) Synovial membrane biopsy. This proved simple, safe, and reliable. All the wounds healed by first intention, and the non-tuberculous patients usually regained full movement. The authors state that although prolonged treatment with streptomycin may alter the histological picture, shorter periods do not appear to produce false negative results. (4) Biopsy of bone. In some cases this examination provided the only proof of tuberculosis. Negative results were of great value in establishing a diagnosis in the non-tuberculous case. Punch biopsy was not used in this series.

The results of each of these investigations are tabulated. [For these the original paper should be consulted.]

Peter Ring

Venereal Diseases

1432. **The Therapeutic Value in Man of a Combination of Trisulphadiazine and Aureomycin.** (L'association trisulfadiazine–auréomycine. Son intérêt actuel en thérapeutique humaine)
J. PILLOT and A. TRIBALAT. *Presse médicale* [*Presse méd.*] **64**, 830–833, May 2, 1956. 28 refs.

The authors argue that the use of an association of antibacterial agents may have many advantages, mainly in reducing the risk of creating drug resistance in the organism concerned and of intolerance and toxic effects in the patient, and possibly in allowing synergic action and widening of the antimicrobial spectrum. They have therefore studied the antimicrobial effects *in vitro* and *in vivo* of combinations of three sulphadiazines with varying amounts of aureomycin on various types of micro-organism. The sulphadiazines were selected on account of the infrequency with which they cause toxic effects and the comparative rarity of natural or acquired resistance to them among the common pathogenic organisms.

Laboratory tests having shown some evidence of synergism against cultures and animal infections of various types, the efficacy of this drug combination was tried in cases of acute and chronic urethritis in males (and also in cases of pulmonary infection and breast abscess). Excellent results are claimed in the treatment of urethritis, both acute and chronic, gonococcal and non-specific [but precise details which would permit comparison with other therapeutic agents are lacking]. The dosage employed was 0·5 to 1 g. of aureomycin with 2 to 4 g. of the triple sulphadiazines daily. Treatment was usually continued for 2 to 3 days and never longer than 6 days.

[The principle of using combinations of antimicrobial agents is generally accepted, and further investigations to determine the optimum proportions of synergistic drugs may well prove profitable, especially in the treatment of chronic genito-urinary infections with a mixture of organisms.] *Robert Lees*

1433. **The Indication for and Limitations of the Treponemal Immobilization Test (Nelson Test).** (Indications et limites du test d'immobilisation des tréponèmes pâles (test de Nelson))
J. DELACRÉTAZ. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 645–648, June 2, 1956. 27 refs.

From his experience with the treponemal immobilization (T.P.I.) test at the University Skin Clinic, Lausanne, the author suggests two major indications for its performance: (1) in patients who give a positive reaction to one of the standard serological tests but show no evidence of syphilis; and (2) in patients who are suspected of having late syphilis but in whom standard serological reactions are negative. He found that the T.P.I. test was highly specific for syphilis and the treponematoses, and considers that a negative T.P.I. test result in patients with treated syphilis may be evidence of cure, although a persistent positive test result is not in itself an indication for further treatment. The exact significance of the latter finding remains as yet uncertain.
G. W. Csonka

1434. **The Use of a Medium Containing Freeze-dried Rat Embryo Extract in the Nelson–Mayer Test.** (Sulla realizzazione del test di Nelson–Mayer con l'uso del terreno all'estratto embrionario di ratto liofilizzato)
V. RESTA and C. ROSSETTI. *Minerva dermatologica* [*Minerva derm. (Torino)*] **31**, 147–149, May, 1956.

The authors point out that in performing the Nelson–Mayer test it has been necessary up to now continuously to renew the rat-embryo extract used in the medium and that this provision has been precariously dependent on a supply of rats in advanced pregnancy. The rate of treponemal survival in the medium as currently used has been such that fresh rat embryos were required every 14 days.

At the University Dermatological Clinic, Padua, the authors have carried out Nelson–Mayer tests in parallel using media containing lyophilized and fresh rat-embryo extracts on negative and positive sera with inactivated and non-inactivated complement, and on saline controls. Only the tests using positive sera and active complement gave complete immobilization. The tests were repeated at fortnightly intervals over 10 months with aliquot portions of the original batch of freeze-dried embryo extract. It was found that such an extract maintained its suitability for the test, and even a slight superiority over the standard medium, throughout the whole period.
F. Hillman

1435. **Deviating and Flocculating Antilipoidal Reagins in Syphilitic Serum.** (Contributo allo studio delle reagine antilipoidee devianti e flocculanti nel siero sifilitico)
R. PEZZI and C. C. BERTANI. *Bollettino dell'Istituto sieroterapico milanese* [*Boll. Ist. sieroter. milan.*] **35**, 137–148, March–April, 1956. 19 refs.

Stating that there is chemical, serological, and clinical evidence for regarding flocculating and complement-deviating antibodies as distinct types, the authors describe studies carried out at the Istituto Sieroterapico Belfanti, Milan, to elucidate this question and to determine whether the complement-fixing antibody is an incomplete antibody in Race's sense—that is, a blocking antibody producing agglutination in a medium with high protein concentration and giving a positive reaction to the Coombs test.

Flocculation tests with VDRL antigen were carried out on samples of syphilitic serum. After centrifugation

a complement-fixation test carried out on the clear supernatant fluid gave a positive result, whereas the same test on the deposit gave a negative one. It is therefore deduced that the complement-fixing antibody does not combine with the flocculating antigen. In a second series of experiments the floccules were washed with sulphuric ether to remove all lipids and cholesterol. The washed floccules then again gave a positive (but weaker) reaction to the flocculation test and also to the complement-fixation test. Thus the flocculating antibody is able to deviate complement.

Flocculation tests were also carried out on sera to which an equal quantity of a 30% solution of albumin had been added. Neither the floccules filtered off nor the supernatant in this series gave a positive reaction to the complement-fixation test. Thus it appeared that the complement-deviating antibody flocculated in the high-protein medium like an incomplete antibody. Finally, when serum which gave a positive complement-fixation reaction only and a negative result in the flocculation test was added to flocculation-positive sera it prevented flocculation in these sera. Performance of the Coombs test on these blocking sera gave a negative result—possibly, however, owing to the sequence in which the tests were carried out.

It is concluded that complement-fixing and flocculating antibodies represent two distinct types of antibody. The authors recommend that until the clinical inferences to be drawn from these facts are understood, both the complement-fixation and flocculation tests should be applied. *F. Hillman*

1436. **Results of Five Years of Penicillin Treatment of Neurosyphilis.** (Ergebnisse 5jähriger Penicillin-Behandlungen bei Neurosyphilitikern)
T. Orbán and L. Lazarovits. *Wiener medizinische Wochenschrift* [*Wien. med. Wschr.*] **106**, 377–381, April 28, 1956. 2 figs., 20 refs.

From the University Neurological Clinic, Budapest, the authors report the results of treatment of 254 patients with neurosyphilis during the 5-year period 1949–54. Of these patients 56 (22%) had meningo-vascular syphilis, 74 (29%) asymptomatic neurosyphilis or pupillary abnormalities only, 60 (24%) dementia paralytica or taboparesis, and 64 (25%) tabes dorsalis. Examination of the cerebrospinal fluid (C.S.F.) was carried out once every year up to 1953 and afterwards at intervals of 6 months.

In 189 cases treatment was with penicillin alone and in 65 with penicillin and fever therapy. During 1949 penicillin was given in courses to a total dose of 3 to 4·8 mega units each, but after that date this was increased to provide a total of 6 to 9 mega units. [Most of the patients appear to have received more than one course of penicillin.]

The effects of penicillin alone and of penicillin plus fever therapy are compared. Penicillin alone produced the best results in meningo-vascular syphilis, improvement in the C.S.F. findings occurring in 98% of these cases and clinical improvement in 22·5%. Of the patients with tabes dorsalis 5·5% showed clinical deterioration after treatment with penicillin despite marked improvement in the C.S.F. In the patients with dementia paralytica and tabo-paresis the results of combined therapy with penicillin and fever were better than with penicillin alone. Relapses, as indicated by the C.S.F. findings, occurred in 16% of the patients treated with penicillin alone but in only 2% of those treated with penicillin plus fever. Among the tabetics, although combined penicillin and fever therapy produced a more rapid improvement in the C.S.F. picture, progression of the disease occurred twice as frequently in this group as in tabetic patients treated with penicillin alone. Patients with lightning pains did better on penicillin alone, fever therapy seeming to precipitate attacks of these pains. Of the patients with ataxia 64% improved on treatment with penicillin alone, whereas combined therapy had a tendency to cause deterioration. There were 8 patients with optic atrophy and these were treated with penicillin alone, 5 showing objective and subjective improvement, but in 3 the condition remained stationary throughout the period of observation.

In conclusion the authors suggest the following doses of penicillin for the treatment of neurosyphilis: in late asymptomatic and meningo-vascular neurosyphilis 6 to 12 mega units, and in dementia paralytica and tabes dorsalis 12 to 20 mega units. Fever therapy is recommended in cases where penicillin does not produce clinical improvement or in which the C.S.F. does not return to normal after a reasonable period. Fever therapy is further recommended in cases of dementia paralytica, tabo-paresis, and progressive optic atrophy. *R. D. Catterall*

1437. **Third Generation Syphilis.** (Die Lues der dritten Generation)
L. Szegö. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **133**, 560–567, June 2, 1956. 1 fig., bibliography.

After a short review of the literature on third generation syphilis the author describes a case seen at the Komitatsspital, Nyiregyhaza, Hungary. Only 68 such families which conformed to the strict criteria laid down by Finger and Fournier have been described. In the author's case a 41-year-old mother and her 6-year-old daughter were found to have congenital neurosyphilis. The child's maternal grandmother was known to have had many miscarriages and only her 3 youngest children survived, all of whom had congenital syphilis. The husband of the mother (the child's father) was found to be free from syphilitic infection. Some syphilitic stigmata were found in both mother and daughter and it is thought noteworthy that the main lesions in both cases were confined to the central nervous system, suggesting that some constitutional factor influencing the site of the lesions may have been concerned. *G. W. Csonka*

1438. **Neurosyphilis Treated with Achromycin in a Penicillin-sensitive Patient.** (Achromycinbehandlet neurolues hos penicillin-overømfintlig pasient)
A. Voll. *Tidsskrift for den Norske Lægeforening* [*T. norske Lægeforen.*] **76**, 474–475, July 1, 1956.

Tropical Medicine

1439. **Skimmed Milk and Kwashiorkor**
P. J. PRETORIUS, J. D. L. HANSEN, J. G. A. DAVEL, and J. F. BROCK. *South African Medical Journal* [*S. Afr. med. J.*] **30**, 447–450, May 12, 1956. 1 fig., 17 refs.

In continuation of their previous comprehensive study of kwashiorkor in South Africa (*Lancet*, 1955, **2**, 355; *Abstracts of World Medicine*, 1956, **19**, 200), the authors now report a further investigation of various types of skimmed milk, which is becoming generally recognized as the dietary supplement of choice in the treatment of kwashiorkor. Groups of cases, totalling 135, each received one of the following preparations: (1) an imported spray-dried lactic acid skimmed milk supplied in air-tight containers; (2) a locally made roller-dried brand packed in bags not impervious to moisture; (3) the same with added vitamin supplements; and (4) fresh skimmed milk with vitamin supplements.

From this study the authors conclude that added vitamin supplements do not hasten the recovery rate, and that the imported spray-dried brand of skimmed milk was superior to the others tested. If the essential lack in kwashiorkor is amino-acids rather than vitamins, then the importance of high standards of preparation and packing of skimmed milk is evident, for heat and moisture may inactivate lysine and other amino-acids in the milk. *Clement C. Chesterman*

1440. **Schistosomiasis of the Liver. Clinical, Pathologic and Laboratory Studies in Egyptian Cases**
M. RAGHEB. *Gastroenterology* [*Gastroenterology*] **30**, 631–660, April, 1956. 26 figs., bibliography.

At the University Hospitals, Cairo, clinical findings were correlated with the histological findings in liver tissue obtained by needle biopsy, and with the results of liver function tests in 125 cases of schistosomiasis in which hepatic enlargement was associated with either urinary or intestinal infection, as demonstrated by the presence of ova; cases with additional diseases, such as amoebiasis or malaria, that might affect the liver were not included. Ova of *Schistosoma haematobium* were found in 76 cases and those of *S. mansoni* in 49, dual infection being present in 18 cases.

The 125 cases fell into two groups, those with ascites (53 cases) and those without (72 cases). The size of the liver and spleen was usually greater in the ascitic cases and provided more marked clinical evidence of collateral circulation, and there was a higher incidence of haematemesis and oedema of the lower limbs. All but one of the cases were examined by sigmoidoscopy and mucosal lesions were found in 89%. It is of interest that since *S. haematobium* was present alone in 60·8% of cases, these intestinal lesions cannot be ascribed to *S. mansoni* only. It was not possible to obtain good liver biopsy material in some cases with marked ascites, but of the 78 cases successfully examined, 11 (14%) showed no pathological changes, only 16 (20·5%) showed schistosome ova, and in the remainder the principal changes were periportal inflammation and fibrosis, other findings being granuloma, diffuse fibrosis, and changes in the parenchyma. The small number of cases in which ova were demonstrated does not commend needle biopsy as a method of diagnosis. Several of the liver function tests indicated marked hepatic disturbance, but it is considered that the only definite correlation was that between the degree of fibrosis and the result of the "bromsulphalein" retention test. *O. D. Standen*

1441. **An Experiment in the Control of Schistosomiasis**
G. MACLEAN. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **50**, 81–84, March 1956. 9 refs.

In a previous report (*Ann. trop. Med. Parasit.*, 1954, **48**, 21; *Abstracts of World Medicine*, 1954, **16**, 295) an account was given of an attempt to control the incidence of genito-urinary schistosomiasis in the population of the island of Likoma in Lake Nyasa. The author now describes the work done and results achieved from June, 1952, up to the end of 1954.

Attempts at sanitary education through the distribution of pamphlets and the establishment of village health committees were of little value in control. Systematic destruction of snails by poisoning in areas normally frequented by the population resulted in a temporary reduction in the number of snails, but some small foci were missed and only in some temporary pools was permanent eradication achieved. Concurrently with these measures mass therapy with "nilodin" (lucanthone; miracil D) was continued. Of the patients treated before 1952, 818 were followed up, and of the 683 on whom more than one examination was made, the results were negative on each occasion in 86·5%. Of the 683, 209 were examined in 1952, 1953, and 1954, with negative results on each occasion in 86·12%. Nilodin is considered to be suitable for mass treatment in spite of its unpleasant taste and transitory side-effects.

The author points out the danger that mass treatment with nilodin might produce a drug-resistant strain of parasite, and considers that those patients who fail to respond to treatment with this drug should receive some other specific. It is suggested that trivalent sodium antimony gluconate may be of special value for this purpose because of the short course of treatment necessary. [In a personal communication to the abstracter, the author confirms that the reference in the original paper to trivalent sodium antimony tartrate in this connexion is an error which will be corrected in a subsequent issue of the journal.] Of the 42 cases treated, 14 have been followed up. Of these, 3 remained infected.

In population surveys up to January, 1952, 27·56% of 3,468 persons were found to be infected; in 1952 and 1953, 10·42% of 2,500 persons gave a positive diagnosis, while in 1954 examination of 1,520 persons showed only 7·83% to be infected. *O. D. Standen*

Allergy

1442. **Pneumothorax, Mediastinal Emphysema, and Spontaneous Subcutaneous Emphysema in Asthmatics.** (Pneumothorax, emphysème médiastinal et emphysème sous-cutané spontanés chez l'asthmatique)
J. TURIAF, P. MARLAND, and H. MATHIEU. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **10**, 117–167, 1956. Bibliography.

The authors give a detailed description of 12 cases of spontaneous pneumothorax (8 generalized, 4 partial) and 3 of mediastinal and subcutaneous emphysema occurring among some 2,000 cases of asthma seen during the past 10 years, and on the basis of their experience discuss the clinical features and significance of these conditions. Of the 15 patients, 12 were males, and their average age was 42 (range 17 to 65).

Unless frequent radiographs are taken and emphysema is regularly sought by palpation of the skin the occurrence of these complications passes unnotlced in many cases. In other instances, however, the patient suffers sudden violent pain in the chest or develops extreme dyspnoea, cyanosis, and signs of acute heart failure. Spontaneous pneumothorax in the asthmatic occurs more commonly on the left than on the right side and, like mediastinal or subcutaneous emphysema, is generally benign. Of the authors' cases, 12 healed spontaneously within 7 to 30 days, though one death occurred following bilateral spontaneous pneumothorax and a second in a patient with long-standing respiratory insufficiency which was aggravated by the development of unilateral pneumothorax. Pneumothorax was recurrent in 2 cases, occurring 5 times in 5 years, always on the left side, in one, and 3 times in 2 years, twice on the left and once on the right side, in the other. The recurrences were characterized by absence of thoracic pain, and by very much slower absorption. Six cases of hydropneumothorax were encountered in this series, the clinical signs being few and the fluid scanty in amount, but rich in eosinophil granulocytes, although the eosinophil count in the blood was normal.

Surgery has no place in treatment. The authors recommend the intravenous administration of theophylline in mild cases, with simple analgesics for the relief of thoracic pain. When dyspnoea is severe and prolonged they advise (1) the withdrawal of 300 to 400 ml. of blood, and (2) the slow infusion over 3 to 4 hours of 12·5 mg. of ACTH in 250 ml. of isotonic glucose solution, repeated twice daily for 4 to 5 days and then replaced by oral cortisone. This treatment was used with success in one case.

The authors consider that these complications of asthma have a common mechanism, in which the two essential factors are weakening of the alveolar walls and abnormal variation in intra-alveolar pressure. Evidence of the former was provided in 6 of their 15 cases in the form of circumscribed areas of localized emphysema and emphysematous bullae. They consider that the danger of spontaneous pneumothorax is not so great during bouts of coughing as during the inspiratory phase following forced expiration, when the difference between the alveolar and pleural pressures increases.

E. S. Wyder

1443. **Treatment of Seasonal and Perennial Allergic Rhinitis with Prednisone and Prednisolone**
E. B. BROWN and T. SEIDEMAN. *Journal of Allergy* [*J. Allergy*] **27**, 305–311, July, 1956. 1 fig., 2 refs.

The authors report from Montefiore Hospital, Bronx, New York, the results of the treatment with prednisone or prednisolone of 79 allergic patients who had had no previous treatment or who had not responded to routine measures; 73 were suffering from ragweed hay fever and 6 from perennial allergic rhinitis. In 75 of the 79 patients an excellent or good result was obtained, whereas only 19 of 78 similar patients not so treated experienced the same degree of relief. The total dosage varied between 40 and 380 mg., the daily dose from 20 to 40 mg., and the duration of treatment from 2 to 32 days. Some of the patients were able to discontinue the treatment before the end of the pollen season. In only one case were gastro-intestinal symptoms so severe that the treatment had to be stopped.

H. Herxheimer

1444. **Bronchoconstrictor Agents and their Antagonists in the Intact Guinea-pig.** [In English]
H. HERXHEIMER. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **106**, 371–380, June 1, 1956. 12 refs.

The antagonistic effect of atropine, propantheline, hexamethonium, adrenaline, papaverine, aminophylline, chlorpromazine, mepyramine, cocaine, and LSD [lysergic acid diethylamide] against the bronchoconstrictor action caused in the intact guinea-pig by the inhalation of histamine, acetylcholine, methacholine, nicotine, "furmethide", and 5-hydroxytryptamine aerosols has been investigated. Atropine, propantheline, and hexamethonium antagonize all these bronchoconstrictors. The first two act more strongly against the acetylcholine group, whilst hexamethonium, cocaine, and adrenaline antagonize nicotine more strongly than any other substance. Mepyramine and LSD antagonize exclusively histamine and 5-hydroxytryptamine respectively. Aminophylline, papaverine, and chlorpromazine antagonize all bronchoconstrictors equally well. The antagonism of hexamethonium against histamine suggests that ganglionic mediation is involved in the action of histamine. Its action against anaphylactic shock suggests that the nervous elements of the bronchial membrane play some part in the symptoms of anaphylaxis. LSD increased the bronchoconstrictor action of all substances except that of 5-hydroxytryptamine.—[Author's summary.]

Nutrition and Metabolism

1445. **Investigations on the Influence of Diet on the Quantity and Composition of Intestinal Gas in Humans**
F. ASKEVOLD. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] 8, 87–94, 1956. 25 refs.

Physical comfort being of primary importance to flying personnel, an investigation was carried out by the Medical Service of the Royal Norwegian Air Force into the relation between diet and the quantity and composition of gas formed in the intestines, changes in the volume of which due to rapid changes of altitude may give rise to various symptoms. Rectal gas was collected continuously for 10 hours each day for periods of 8 days from 3 schizophrenic, demented women whose appetite was normal and physical state healthy, the volume of gas and its content of oxygen, carbon dioxide, methane, and hydrogen being determined. The author points out that the quantity and composition of the gases are altered during intestinal passage as a result of diffusion, which is itself influenced by the rate of passage and other factors, and that therefore " the rectal gases afford only a rough approximation of what has taken place in the upper regions of the intestines ". The subjects were first given a liquid, cellulose-free, basic diet, to which were added, in turn, carrots, cabbage, dried peas, potatoes, wholemeal bread, white bread, lean meat, fat meat, and fish. Finally, two mixed diets were administered. Each diet was given for 3 days before gas collection was started, two 4-day collections being made, separated by a 3-day rest period.

No single food added to the basic diet had any significant effect on the quantity or composition of the rectal gas. A mixed diet rich in both fat and vegetables, however, produced a slightly higher total volume, which is attributed partly to increased peristalsis, partly to " a real increase in the proportion of fermentation gases ". It is concluded that diet has no definite influence on the quantity and composition of rectal gas.

Joseph Parness

1446. **An Experimental Test of the Glucostatic Theory of Regulation of Food Intake**
L. M. BERNSTEIN and M. I. GROSSMAN. *Journal of Clinical Investigation* [*J. clin. Invest.*] 35, 627–633, June, 1956. 2 figs., 20 refs.

Many theories have been propounded to explain appetite and the regulation of food intake, of which the most widely accepted at present is the " glucostatic " theory of Mayer. He suggests that appetite depends on the sensitivity of an appetite centre, probably in the hypothalamus, to its own rate of glucose utilization, a slow rate causing hunger sensations and the taking of food and a high rate giving the sensation of satiety.

In experiments at Fitzsimons Army Hospital, Denver, Colorado, the authors studied the relation between the blood glucose level and the subjective sensation of appetite and the rate of voluntary food intake. In the first experiment 9 young men aged 19 to 22 were each given five different test treatments, four of them on two occasions, in random order on different days 4 hours after a standard breakfast. Normal saline and 25% glucose solution (200 ml.) were each given by stomach tube and intravenously twice, and 10 mg. of amphetamine in 200 ml. of saline by stomach tube once. Thirty minutes after the treatment the subject was allowed to eat freely from a variety of attractive foods, and the food intake was measured. Samples of venous and capillary blood were taken for the determination of glucose content just before the test treatment, just before the meal, and 30 minutes later. The blood glucose level was not affected by the administration of saline by either route or of amphetamine. The intravenous injection of glucose caused a bigger rise in the glucose content of both arterial and venous blood than intragastric administration, and a bigger difference between arterial and venous levels (the A-V difference, which provides an index of glucose utilization). Thus the arterial and venous glucose levels and the A-V difference were all quite different after the five different treatments, but in spite of this the total food intake and the intake of protein, fat, and carbohydrate were the same, on average, whatever the treatment.

In the second experiment the subjects were the same 9 men together with 3 others. Each was given, three times, each of four treatments—intravenous and intragastric saline and glucose—4½ hours after a standard breakfast, and at intervals from before breakfast until 1½ hours after treatment they were asked whether they were hungry and to what extent, the responses being scored on a scale ranging from 1 for " no desire to eat" to 5 for " extremely hungry ". Appetite was highest just before breakfast, fell to a low level immediately after breakfast, and then rose steadily for the next 6 hours. There was no difference in appetite following the different treatments.

John Yudkin

1447. **An Investigation of the Rarity of Infantile Scurvy among the South African Bantu**
M. ANDERSSON, A. R. P. WALKER, and H. C. FALCKE. *British Journal of Nutrition* [*Brit. J. Nutr.*] 10, 101–105, 1956. 12 refs.

It has been previously observed that Bantu children are remarkably free from signs of scurvy, although in the great majority, particularly in urban areas, the intake of ascorbic acid (vitamin C) is very low. In the investigation here reported from the Coronation Non-European Hospital, Johannesburg, no clinical or radiological evidence of scurvy could be found in 33 urban Bantu infants admitted to the hospital with severe malnutrition or other illnesses or in 29 infants attending the out-

patients' department; all the children were under 2 years of age. Plasma ascorbic acid levels were within normal limits, although inquiry showed that the diet contained very little ascorbic acid, the daily intake of the vitamin in many cases being calculated to be less than 3 mg. The authors discuss these findings and suggest that they would seem to indicate that the possibility of endogenous production of the vitamin cannot be ruled out.

F. W. Chattaway

1448. **The Influence of Vitamin B_{12} and Aureomycin upon the Growth of Protein-deficient Children**

I F. S. MACKAY, S. J. PATRICK, D. STAFFORD, and F. S. CLEVELAND. *Journal of Nutrition* [*J. Nutr.*] **59**, 155–170, May 10, 1956. 26 refs.

In a study carried out at University College of the West Indies, Jamaica, after the heights and weights of 2,012 protein-deficient Jamaican children aged 4 to 16 years and of both sexes had been measured, 523 of them were selected, on the grounds of similarity of growth records, sex, and locality, for investigation of the effect of vitamin B_{12} (cyanocobalamin) and aureomycin on their growth. The children were divided at random into four groups, which received respectively: (1) a placebo, (2) 65·3 μg. of cyanocobalamin, (3) 31·7 mg. of aureomycin, and (4) 64 μg. of cyanocobalamin plus 32 mg. of aureomycin, in each case per head daily. [The duration of the period of supplementary feeding is not stated.] Clinical examinations were carried out before and after the supplementation, and the serum total protein, serum albumin, and serum cholinesterase levels and haemoglobin value were determined 9 to 12 months after the supplementation was started, while in 165 cases a precise dietary survey was made.

Except for a slight acceleration in the rate of weight increase in those given aureomycin, neither supplement had any effect. The dietary survey revealed the following mean daily intakes: 1,686 Cal., protein 47 g., calcium 284 mg., iron 13·5 mg., vitamin A 1,648 I.U., thiamine 0·92 mg., and ascorbic acid 119 mg. The clinical examination indicated a state of " marginal malnutrition ", cheilosis, stomatitis, dry skin, caries, odontoclasia, follicular keratosis, and palpable liver being common. It is concluded that neither of the supplements investigated " would be of practical value in alleviating the malnutrition found in such areas as the Caribbean ".

H. E. Magee

1449. **Phenmetrazine in the Management of Obesity**

E. P. GELVIN, T. H. MCGAVACK, and S. KENIGSBERG. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **1**, 155–159, April, 1956. 4 refs.

The sympatheticomimetic drug " phenmetrazine ", which is related to amphetamine, was given in doses of 25 mg. three times a day to 53 patients, all but one of them women, attending the Obesity Clinic of the Welfare Island Dispensary, New York. Alternate patients received a placebo initially, the two substances being interchanged after a course of 6 weeks, the patients thus acting as their own controls. The double-blind technique was used. All patients were restricted to a reducing diet providing 1,000 Cal. daily. The average weight loss per week of the test group was 0·9 lb. (0·4 kg.), while that of the control group was only 0·3 lb. (0·13 kg.). Side-effects were infrequent. The authors consider that the effect of phenmetrazine is due to depression of the appetite rather than to any direct effect on metabolism.

R. Schneider

1450. **The Relationship between Plasma Sodium Concentration and the State of Hydration of Burned Patients**

H. S. SOROFF, E. PEARSON, E. REISS, and C. P. ARTZ. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 472–482, April, 1956. 7 figs., 3 refs.

Hyponatremia is characteristic of adequately treated burns. It appears to be caused, at least in part, by dilution. It is asymptomatic and can be considered a part of the normal, satisfactory response to a burn. Hypernatremia often occurs in the presence of clinical signs and laboratory evidence of intracellular dehydration. The condition is associated with a lowered urinary volume. After 48 hours, the administration of large quantities of nonelectrolyte water is essential to meet the water requirements of severely burned patients. The plasma sodium concentration is a good index of the adequacy of hydration. The gradual redistribution and excretion of edema fluid in extensively burned patients and the lack of evidence of pulmonary edema in patients observed emphasize the safety of maintaining an adequate water intake after 48 hours.—[Authors' summary.]

1451. **Relation between Caloric Intake, Body Weight, and Physical Work: Studies in an Industrial Male Population in West Bengal**

J. MAYER, P. ROY, and K. P. MITRA. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 169–175, March–April, 1956. 1 fig., 16 refs.

Experiments with rats have shown that the relationship between physical activity and food intake is a straight line over only a relatively restricted range of activity (" normal activity range "). When bodily activity is reduced to a low level (" sedentary zone ") the food consumption of rats does not fall further, but in fact increases slightly.

The investigation here reported was carried out on 213 workers at a jute mill at Chengail, West Bengal, whose weight was known and who were between 5 ft. 2 in. (1·58 m.) and 5 ft. 4 in. (1·62 m.) in height. They were apparently well and had no obvious signs of malnutrition. Food intake was judged from replies to questions at an interview, which were checked against food purchases and storage. Because of the uniformity of the diet and the fact that little food was stored, the reliability of this method of recording food intake was much higher than would be the case in a Western population. The workers were divided into five groups according to physical activity—sedentary, light work, medium work, heavy work, and very heavy work. Many correlations were sought between calories and nutrients on the one hand, and religion, age, income, and physical activity on the other. The only important relationship which emerged was between calorie intake and physical

activity. All except the sedentary group were of similar body weight, and their intake of calories increased with physical activity. Sedentary workers on the other hand were, on the average, heavier than those in the other groups; the average calorie intake in the sedentary group was higher than that in the groups doing light work, medium work, and heavy work, and was only lower than that of the group doing very heavy work.

The authors conclude that sedentary occupation, an "unnatural" recent development in man's social evolution, may well play a large part in the increased incidence of obesity. *John Yudkin*

1452. **Diet and Serum Cholesterol in Man: Lack of Effect of Dietary Cholesterol.**
A. KEYS, J. T. ANDERSON, O. MICKELSEN, S. F. ADELSON, and F. FIDANZA. *Journal of Nutrition* [*J. Nutr.*] **59**, 39–56, May 10, 1956. 26 refs.

An account is given of prolonged investigations into the relation between the dietary cholesterol content and the serum cholesterol level which were carried out on physically healthy male subjects aged 20 to 60 years in Minnesota and in Sardinia. From a series of 286 clinically healthy men who had been studied annually by the authors at the University of Minnesota since 1947, a group of 33 whose job, diet, and body weight had remained constant over a period of 4 years and whose dietary cholesterol intake was low was selected and the average blood cholesterol level compared with that of a comparable group of 35 men whose diet was very high in cholesterol; there was no significant difference in serum cholesterol level between the two groups. In the same population there were 64 men whose dietary cholesterol intake had undergone a major change (that is, had increased or decreased by 50% or more) for various reasons without any major change in body weight. No effect on the average serum cholesterol level was detected 4 to 12 months after the change in diet.

In completely controlled experiments on groups consisting of 5 to 7 physically healthy schizophrenic patients it was shown that the addition to or removal from the diet of 500 to 600 mg. of cholesterol daily had no effect on the reduction in the serum cholesterol level produced by a diet of rice and fruit; nor could any rise or fall in the serum cholesterol content be observed on changing from the rice–fruit diet to ordinary diet or vice versa. In another controlled experiment an increase in the daily cholesterol intake from 374 to 1,369 mg. had no significant effect on the serum cholesterol level of 13 men with a daily dietary fat intake of 66 g., while the reverse change in a similar group of 12 men was equally without effect.

In surveys carried out in the island of Sardinia, where the population exists on a very simple diet which is very low in cholesterol content, doubling or trebling the dietary cholesterol intake of two groups of men had no effect on the serum cholesterol level.

It is concluded that in man the serum cholesterol content is essentially independent of cholesterol intake "over the whole range of natural human diets". *Z. A. Leitner*

1453. **Vitamin-A Levels in Idiopathic Hypercalcaemia**
W. M. FYFE. *Lancet* [*Lancet*] **1**, 610–612, May 5, 1956. 10 refs.

As part of an investigation of vitamin-A deficiency in infancy at the Royal Hospital for Sick Children, Glasgow, the plasma vitamin-A levels were determined in 7 healthy children and 8 infants with idiopathic hypercalcaemia before and after a large dose of vitamin A by mouth. In the infants with hypercalcaemia the fasting vitamin-A level was about double that in the controls; 4 hours after oral administration of the standard dose of vitamin A the level in these infants was three times as high as that in the controls. In 5 infants who were marasmic from other causes the plasma vitamin-A level was not raised unduly. *H. Harris*

1454. **Cephalin-lipidosis. A New Disorder of Lipid Metabolism.** [In English]
H. S. BAAR and E. M. HICKMANS. *Acta medica Scandinavica* [*Acta med. scand.*] **155**, 49–64, June 30, 1956. 12 figs., bibliography.

The authors report their findings in 2 cases of a hitherto undescribed disease studied at the Children's Hospital, Birmingham, in a brother and sister who died at 4 and 6 years of age respectively, both from bronchopneumonia. The main features of the disease during life were almost identical, consisting in mental retardation and splenomegaly.

Histologically, there was accumulation of a lipoid substance in the splenic reticulum cells, in the Kupffer cells, and in the neurones of the cerebral cortex, central grey matter, and spinal cord, and also in a few cells in the bone marrow and kidney. Chemical analysis in one case showed a rise in the cephalin and a fall in the lecithin content of the spleen, liver, kidneys, and whole blood compared with normal controls.

That the stored substance contained lipid was shown by its sudanophilia, and it was positive to Baker's test for phosphatides. The presence of polysaccharide was shown by a positive periodic-acid–Schiff reaction. The presence of reducing groups was excluded by negative Schmorl, performic-acid–Schiff, and peracetic-acid–Schiff reactions. The substance was not metachromatic, and as only weak metachromasia was induced by sulphation, the polysaccharide was presumed to contain only a few hexose units. The possibility that the material was an inositol-containing phosphatide was suggested by its solubility characteristics and by the negative or atypical reactions obtained with histochemical tests for other phosphatides. Analysis of the major splenic lipid fraction gave a nitrogen:phosphorus ratio of 2:1, and this, together with the high methylene-blue extinction value observed histochemically, suggested that the inositol, if present, was aminated to inosamine. The latter substance was therefore synthesized and a chromatographic comparison made with hydrolysed splenic lipid, which contained a component of identical mobility.

The authors conclude that the stored substance in these cases was a cephalin containing inosamine, and propose a formula for it. *M. C. Berenbaum*

Gastroenterology

1455. **Belladonna Alkaloid–Sedative Mixture. Effects on Gastric Acidity and Motility**

F. STEIGMANN and L. KAMINSKI. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **1**, 174–189, April, 1956. 7 figs., 17 refs.

The effect of "donnatal", a mixture of "natural belladonna alkaloids" and phenobarbitone, was studied in 176 patients in or attending Cook County Hospital, Chicago, with various gastro-intestinal disorders. Secretory studies showed that spontanous gastric acid secretion and secretion after histamine stimulation were unaffected. Antral motility was depressed in 8 out of 12 patients, such depression occurring after a latent period ranging from 3 to 74 minutes.

Clinically, of 78 patients with peptic ulcer, over three-quarters obtained symptomatic relief, as did all of 6 female patients with "gall-bladder disease" and 3 out of 5 patients after operation for carcinoma of the colon. Those with ulcerative colitis, amoebiasis, and "irritable bowel" did less well. Side-effects of the drug were negligible, consisting chiefly in drowsiness and dryness of the mouth. Symptomatic relief was sometimes, but not always, accompanied by depressed gastric motility.

[This paper contains no accurate data regarding dosage, the amounts given being expressed only as "tablets".]

R. Schneider

1456. **The Blood Groups in Peptic Ulceration**

D. A. PEEBLES BROWN, A. G. MELROSE, and J. WALLACE. *British Medical Journal* [*Brit. med. J.*] **2**, 135–138, July 21, 1956. 11 refs.

Certain important differences exist, both in the prevalence of peptic ulcer and in the distribution of ABO blood groups, between Scotland and England. At the Western Infirmary and Southern General Hospital, Glasgow, the authors have carried out a survey of the ABO Rh(D) blood-group distribution in 2,059 patients with proved peptic ulcer. In 1,177 cases the ulcer was seen at operation, and in the remainder a chronic peptic ulcer had been demonstrated by barium-meal examination. The blood groups were determined on freshly collected venous blood samples, the ABO group by testing both cells and serum, the Rh(D) group with two potent agglutinating sera. A control was provided by comparison with the blood groups of 5,898 consecutive new blood donors registered at the West of Scotland Regional Blood Transfusion Centre, Glasgow.

Among the patients with all types of peptic ulcer there was a significant increase in the proportion of those possessing blood of Group O, whereas the distribution of the Rh(D) group among 1,606 patients did not differ significantly from that in the controls. In patients with duodenal ulcer (including juxtapyloric ulcer) there was a significantly higher proportion belonging to Group O than there was in the control series, and this excess was greater in those cases confirmed at operation than in those diagnosed only radiologically. The authors suggest that examination of a larger series would be required to confirm or refute the possibility that there is a relationship between the excess of Group-O patients and the severity of the duodenal ulcer. The blood-group distribution among patients with gastric ulcer did not differ from that in the controls, but patients with stomal ulcer showed a greater percentage increase of Group O compared with controls than did any other sub-group.

In a subsidiary investigation of a possible relationship between the possession of blood of Group O and excess output of gastric acid the augmented histamine test was carried out on 276 patients; no correlation was noted between the maximum acid output and blood group in patients with either gastric or duodenal ulcer.

T. J. Thomson

1457. **Partial Gastrectomy for Peptic Ulceration in the Aged**

W. W. DAVEY and B. O'DONNELL. *Lancet* [*Lancet*] **1**, 1033–1035, June 30, 1956. 1 fig., 6 refs.

In presenting their results in 30 cases of peptic ulcer in patients over 70 years of age operated upon at the Whittington Hospital, London, the authors make a plea for planned gastric resection in patients in this age group when symptoms or complications make it necessary. [Few surgeons would disagree with this view.] They describe their method of caring for the patient in hospital, and state a preference for operating under local analgesia. [Many surgeons would, however, disagree with this, as also with the routine administration of penicillin for 5 postoperative days.] There were no postoperative deaths in this series. All the patients were followed up for one to 5 years after operation, and the results appear to be very satisfactory.

Roland N. Jones

1458. **Vagotomy for Chronic Peptic Ulcer. A Five-year Follow Up**

G. SLANEY, P. G. BEVAN, and B. N. BROOKE. *Lancet* [*Lancet*] **2**, 221–224, Aug. 4, 1956. 3 figs., 3 refs.

This is a follow-up report on 91 patients subjected to vagotomy for chronic peptic ulceration at the Queen Elizabeth Hospital, Birmingham, during the years 1947–9. Of these patients 79 had duodenal ulcer, 5 anastomotic ulcer, 6 gastric ulcer, and one combined gastric and duodenal ulcers. Vagotomy was carried out alone in 74 cases (thoracic 53 and abdominal 21), and combined with gastro-enterostomy in 14 and with pyloroplasty in 3 cases. There was one operative death, and also 4 deaths from unrelated causes. All the survivors, except one who was untraced, were followed up for 5 years.

Ulceration recurred in 24 of the remaining 85 cases (28·2%), and in 18 of the 65 (27·7%) in which no drainage operation had been carried out either before or at the

time of vagotomy. Recurrence of the ulcer could not be correlated with changes in gastric acidity, which was tested immediately before and after vagotomy and at 6 and 18 months. Recurrence took place at varying intervals after the operation, in 6 cases not until 4 to 5 years later. Thus there is reason for assuming that the recurrence rate would have been even higher if the follow-up had been longer. It is of interest that 6 patients who had previously had a duodenal ulcer subsequently developed a gastric ulcer. Of the 5 patients with anastomotic ulcer, one developed recurrent ulcer; and 3 of the 6 cases of gastric ulcer showed evidence of recurrence. There was little difference in the rate of recurrence whether the vagotomy was performed by the thoracic or the abdominal route.

The authors conclude that there may be a place for vagotomy in the treatment of duodenal ulcer in women, 7 of the 8 women in the series remaining well, so that results were proportionally much better than in the men; they recommend the abdominal route in order that the lesion may be inspected. They also consider that vagotomy may be of value in recurrent ulceration where the alternative is total gastrectomy; in these cases the thoracic route is preferable, as previous operation on the abdomen renders exposure of the nerves from below the diaphragm difficult. *T. D. Kellock*

1459. **Antispasmodic Compound 8-88 in Relapsing Peptic Ulcer**

G. B. J. GLASS and M. RICH. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **1** (New Series), 160–173, April, 1956. 9 refs.

Several salts and esters of phenyloxyacetic acid have been shown to relieve spasm of smooth muscle. At the Flower and Fifth Avenue Hospitals, New York, the authors have studied the effect of one of these compounds, (α-N-)-B-diethylaminoethyl-amino-phenylacetic acid-*iso*amylester hydrochloride (Compound 8-88), on 30 patients with radiologically-proven chronic peptic ulcer. The drug had no significant effect on the pattern of the gastric secretion stimulated by the administration of histamine or insulin in 13 patients with duodenal ulcer, and gave no symptomatic relief during the acute stage of an attack nor during a severe relapse. However, out of 16 patients with chronic ulcer who had suffered from frequent relapses during the preceding 2 to 3 years, 12 remained symptom-free for periods of 11 to 13 months; the 4 remaining patients relapsed during treatment with Compound 8-88. The drug was given in doses of 50 mg. four times a day or 100 mg. three times a day; side-effects were negligible. *R. Schneider*

1460. **Psychotherapy in Ulcerative Colitis**

J. W. PAULLEY. *Lancet* [*Lancet*] **2**, 215–218, Aug. 4, 1956. 9 refs.

The author reviews his experience in 48 cases of ulcerative colitis treated with superficial psychotherapy during the past 6 years at the Ipswich Hospitals. He gives in detail 8 striking case histories which showed dramatic improvement when the causes of emotional tension had been discussed and an attempt made to remove them. In 43 cases remission of the presenting attack was obtained with psychotherapy alone, and in 2 others with corticotrophin treatment in addition. There were 2 deaths from perforation and one from electrolytic disturbances consequent upon the use of cortisone to hasten a slow recovery. Of the 42 patients followed up, 31 are completely symptom-free.

The author considers three personality factors to be present in all cases of ulcerative colitis: (1) failure to express anger; (2) dependency; and (3) sensitivity. The external causes of disturbance are nearly always found in the domestic circle as "disturbed personal relationships with their high emotional content". It is recommended that the initial interview should last about half an hour, and be particularly directed to the domestic situation. Relations who may be able to help should be asked to attend at the second interview, which should be held within a week, or sooner in severe cases. As the attack subsides, 10- to 15-minute interviews are arranged at lengthening intervals, but the patient should be able to return at any time if there is a relapse.

The author considers that surgery should be used only when medical treatment and psychotherapy have failed in the genuine chronic case, especially in the young, or in the fulminating case where there is danger of perforation. *T. D. Kellock*

1461. **Carcinoma of the Colon and Rectum Associated with Chronic Ulcerative Colitis**

R. H. THORLAKSON. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **103**, 41–50, July, 1956. 4 figs., 33 refs.

The author describes 12 cases of carcinoma of the colon and rectum found during colectomy in 182 consecutive cases of ulcerative colitis at St. Mark's Hospital, London. This represents an incidence of 6·6%. A review of the literature reveals that this complication has an average incidence of 3% in medically treated cases of ulcerative colitis, but that in surgical series the incidence is higher. The following points emerge from the present study. The average duration of the colitis was 17 years; out of 46 patients with ulcerative colitis lasting more than 10 years carcinoma had developed in 9, whereas only 3 out of the 136 having ulcerative colitis for less than 10 years had developed carcinoma. The average age of the patients with carcinoma was 50 years, or 10 to 15 years lower than that of the general population affected by carcinoma, and females were more often affected than males. The distribution of the carcinomata was of the usual pattern, but multiple growths were frequent. Histologically, 18 of the 23 tumours found were of low grade, and in 7 cases there was no lymphatic spread. Eight out of the 12 patients were alive and well from 2 months to 5½ years after operation. It is probable that early diagnosis contributed to these good results, and in this connexion the difficulty of differentiating a malignant from a simple stricture is stressed. Changes in bowel habit, bleeding, or loss of weight, particularly if occurring during a phase of remission of ulcerative colitis, should arouse suspicions of malignancy.

John Naish

1462. **Respiratory Alkalosis in Hepatic Coma**
P. VANAMEE, J. W. POPPELL, A. S. GLICKSMAN, H. T. RANDALL, and K. E. ROBERTS. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 762–767, June, 1956. 1 fig., 21 refs.

The authors, working at the Sloan–Kettering Institute, New York, have studied some of the biochemical changes which occur in hepatic coma, as seen in 34 patients suffering from liver damage due to metastatic tumour, infection, toxin, or cirrhosis; 29 of the patients were in hepatic coma during the study. In 25 of these patients there was overt respiratory alkalosis, indicated by a raised blood *p*H and a lowered plasma carbon dioxide tension (pCO_2), while the blood ammonia level was raised in all the cases. These changes were found characteristically in the early stages of hepatic coma when hyperventilation was clinically evident, but with the progression of hepatic failure respiratory acidosis and anoxia supervened as a result of depression of the respiration. It is suggested that ammonium may stimulate respiratory exchange in patients with liver failure and that the toxicity of ammonium may be enhanced by a superimposed respiratory alkalosis. It is noted that there was no significant correlation between pCO_2, the blood ammonia levels, and the severity of the condition.
P. C. Reynell

1463. **The Blood Ammonia Level in the Diagnosis of Haemorrhage from the Digestive Tract.** (L'ammoniémie dans le diagnostic des hémorragies digestives)
J. STAHL and R. BOCKEL. *Strasbourg médical* [*Strasbourg méd.*] **7**, 389–398, June, 1956. 4 figs., 15 refs.

The possibility of using the blood ammonia level to distinguish between cases of haemorrhage from the digestive tract due to hepatic cirrhosis from those due to other causes is discussed. In the cirrhotic patient, even in the earliest stages, an increase in the absorption of ammonia from the alimentary tract, as after administration of an ammonium salt, causes an increase in the blood ammonia level, whereas little or no change occurs in the absence of cirrhosis. This may be due partly to the development of the collateral circulation in cirrhosis and partly to inability of the cirrhotic liver to transform ammonia into urea. Ammonia is produced in the distal parts of the intestinal tract by bacterial activity and fermentation of nitrogenous substances, so that the accumulation of blood in the intestine should lead to an increased production of ammonia and, in cirrhosis, a rapid rise in the blood ammonia level, while no such rise should be observed in the non-cirrhotic subject.

This was confirmed by the authors' observations on 5 cases of cirrhosis and one of Banti's syndrome, in which the blood ammonia content rose to levels ranging from 1 to 2·1 mg. per 100 ml. during the 24 hours after a haemorrhage, whereas in 10 non-cirrhotic subjects suffering from haematemesis or melaena the highest value recorded was 0·75 mg. per 100 ml. They draw the conclusion that in the absence of a significant rise in the blood ammonia level after a haemorrhage into the digestive tract a cirrhotic cause may be ruled out, whereas the occurrence of such a rise is strongly suggestive of cirrhosis, whether the bleeding be from a ruptured vein or from a peptic ulcer, which is of frequent occurrence in cirrhosis. Among the practical advantages of this test are its simplicity, the rapidity with which it can be carried out, and the early appearance of a positive result when cirrhosis is present. It is noted, however, that the administration of antibiotics or of non-absorbable sulphonamides may prevent the formation of ammonia by bacterial action and thus give rise to a false negative result.
E. Forrai

1464. **Primary Biliary Cirrhosis**
I. W. MACPHEE. *Lancet* [*Lancet*] **2**, 109–113, July 21, 1956. 5 figs., 8 refs.

The author presents, from the University of Liverpool, some observations on primary biliary cirrhosis based on the clinical and serial liver biopsy findings in 6 cases. Although the condition is rare it may be more frequent than has been realized, for all these 6 cases were seen within a period of 2 years.

The clinical course, if the patient survives long enough, may be divided into the following three stages, which often merge into one another. (1) The stage of obstructive jaundice due to an intrahepatic cause; this stage may persist with varying intensity for months or even years and may occasionally be preceded by a phase in which no jaundice is apparent, but in which the biochemical and histological changes are similar to those seen in infective hepatitis. (2) The stage of portal hypertension with all its signs, namely, ascites, splenomegaly, haematemesis from oesophageal varices, and bleeding from the rectum, with persistence of the jaundice. (3) A final and usually brief stage of liver failure, showing in addition to the previous signs the usual biochemical changes associated with that condition; death results from hepatic insufficiency. The aetiology of biliary cirrhosis remains obscure.

Examination of the serial liver biopsy specimens revealed two distinct phases of pathological change in the liver cells; these phases merged into each other and overlapped the three clinical stages. The first two of the latter were characterized by a progressive periportal and perilobular fibrosis, while in the third clinical stage regeneration of liver cells in a bile-stained liver was evident; these appearances are described in detail and illustrated in photomicrographs. The condition is a progressive one—the lobules become gradually isolated by fibrous tissue until eventually intrahepatic obstruction of the biliary tract ensues. The diagnosis is essentially one of exclusion, and special attention must be paid to ensuring that no remediable extrahepatic cause of the obstruction is present. The biochemical findings are entirely non-specific, revealing only varying grades of obstructive jaundice and progressive liver failure. The prognosis is hopeless, the condition being one of relentless irreversible change and deterioration, and treatment can only be symptomatic. Various dietetic and medicinal measures have proved useless and radical surgery is considered unjustifiable. Cortisone was tried in 2 of the present cases but was without any beneficial effect.
John Fry

Cardiovascular System

1465. **Advance in the Clinical Evaluation of Aortic Stenosis by Arterial Pulse Recordings of the Neck**
P. W. DUCHOSAL, C. FERRERO, A. LEUPIN, and E. URDANETA. *American Heart Journal* [*Amer. Heart J.*] 51, 861–879, June, 1956. 12 figs., 17 refs.

The authors stress the importance of the diagnosis of aortic stenosis in view of the progress of cardiac surgery, discuss various methods of investigating the function of the aortic valve by means of pulse recordings, and point out the limitations of the methods in current use. They then describe a method of recording the carotid pulse which they have developed at the University Cardiological Centre, Geneva, in which an inflatable cuff around the neck is connected to a differential pneumomanometer. This records the oscillogram at a counterpressure of 10 to 20 mm. Hg, and the findings in normal subjects and in 28 cases of aortic stenosis are described and illustrated, including both severe and mild cases and cases with associated aortic incompetence.

The principal characteristics of the oscillogram in aortic stenosis are a slowing of the upstroke, with superimposed vibrations, a delayed, single summit, and a straightening of the descending limb.

D. Goldman

1466. **The Normal Ballistocardiogram**
L. BROTMACHER. *British Heart Journal* [*Brit. Heart J.*] 18, 145–152, April, 1956. 6 figs., 15 refs.

Ballistocardiograms were recorded at the Cardiff Royal Infirmary by means of a photo-electric direct body pick-up from 200 subjects without cardiovascular disease or other conditions known to affect the ballistocardiogram. According to the criteria established by Dock for this type of apparatus, the records were normal in only 128 subjects, but if the presence of a small number of abnormal complexes in any one tracing and a large final systolic downstroke are regarded as normal variants all but 11 records were normal. Abnormalities occurred more frequently with advancing age.

It is concluded that the ballistocardiogram is of more limited practical value than has been suggested. It can be used in assessing cardiac involvement in generalized diseases and in detecting the acute effects on the cardiovascular system of such agents as tobacco. A diagnosis of heart disease is probable when the ballistocardiogram is grossly abnormal in a young subject with a vertical heart and without aortic unfolding, while a normal ballistocardiogram without respiratory variation, especially in an older person, suggests that the heart is normal.

Gerald R. Graham

1467. **The Ballistocardiogram in Congenital Heart Disease**
E. DONOSO, L. PORDY, Y. Z. YUCEOGLU, J. B. MINOR, K. CHESKY, and S. S. AMRAM. *American Heart Journal* [*Amer. Heart J.*] **52**, 352–358, Sept., 1956. 2 figs., 25 refs.

1468. **The Nature and Clinical Significance of the Wolff–Parkinson–White Syndrome.** (О сущности и клиническом значении электрокардиографического синдрома укороченного *P–Q* и одновременно измененного комплекса *QRS* (синдром Вольф-Паркинсон-Уайта))
A. M. SIGAL. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 52–60, No. 5, May, 1956. 3 figs., 18 refs.

More than 20 years have elapsed since the Wolff–Parkinson–White syndrome was first described, but its nature and clinical significance remain obscure. At first it was regarded as an electrocardiographic curiosity, of no special prognostic value and corresponding to no known lesion. Later it was explained as being the result of abnormal conduction of impulses from the auricle to the ventricle via the adventitious accessory bundle of Kent. But this did not answer the questions why, if the bundle of Kent is always present, it should function only in a few cases, why in many cases atropine can abolish the symptoms, and why some cases show right bundle-branch block instead of left, since according to Kent the bundle is present only on the right side. Recently the very existence of Kent's bundle has been denied by many cardiologists (such as Maxim, Lang, and Pace) and the teaching of Prinzmetal and his co-workers has been more and more accepted, namely, that the basis of this syndrome is an accelerated passage of the sinus impulse through the A-V node, combined with a retardation through one or other branch bundle. This would account for the serious prognosis in many cases seen nowadays (though this was seldom mentioned in the earlier cases).

In the present author's view, some cases are due to spasm of the descending branch of the right coronary artery, which supplies the A-V node and the upper part of the left bundle branch. The anoxia caused thereby reduces the inhibitory function of the node, thus leading to premature stimulation of the ventricle. The administration of atropine relieves the arterial spasm so that the A-V node regains its delaying function and the P–R interval returns to normal. In other cases the condition may be due to focal myocardial sclerosis, which has a similar effect on the A-V node, but these cases are not relieved by atropine. In this latter type the prognosis is of course much graver; but it may be grave in the first type also if the arterial spasm persists long enough to lead to myocardial degeneration. The author concludes that the outlook in this syndrome is by no means so favourable as was formerly believed. Although usually seen in young persons, it can also occur in older patients suffering from atherosclerosis or thyrotoxicosis. Paroxysmal nodal or supraventricular tachycardia often occurs in these patients, and an attack may be fatal; indeed, in the author's opinion it is probable that the rarity of the syndrome in middle age is due to the fact that most of these patients die young. A favourable response to atropine, amyl nitrite, or physical exercise and inter-

mission of attacks of the syndrome are good prognostic signs: persistence of the syndrome indicates organic changes in the nodal tissue, in which case the prognosis is poor. *L. Firman-Edwards*

CONGENITAL HEART DISEASE

1469. **Results following the Creation of Pulmonary Artery Stenosis**
W. H. MULLER and J. F. DAMMANN. *Annals of Surgery* [*Ann. Surg.*] **143**, 816–821, June, 1956. 3 figs., 3 refs.

The authors stress the hazards to life of prolonged high pulmonary arterial pressure. This condition may be secondary to a variety of cardiac lesions, and is usually associated with a large right ventricular output. Some natural protection is afforded by the hypertrophy of the media which takes place in the pulmonary arterioles, but the authors, working at the Universities of Virginia (Charlottesville) and of California (Los Angeles), have devised a method whereby this resistance can be shifted proximally, namely, by the creation of an artificial pulmonary stenosis, the effect of the procedure being to lessen the shunt by lessening the right ventricular output, and so to prevent progression of the changes in the pulmonary arterioles. In effect, the operation consists in making a tuck or fold in the pulmonary artery; the stenotic area so created is then surrounded by reactive polyethylene so that the artery is occluded to approximately 75% of its original diameter.

So far 25 patients have been operated upon in this way since 1951, all of these having severe congenital cardiac defects which were not at the time amenable to any other form of surgery. There were 9 operative deaths and one late death. Considerable improvement was obtained in 11 of the remainder. It was found that a fall of pressure beyond the stenosis after operation was a good prognostic sign. The authors point out that the operation is only a palliative one, but suggest that it has a place in the treatment, for example, of patients with a single ventricle, for whom there is as yet no form of surgical treatment available. *J. R. Belcher*

1470. **Clinical and Physiologic Aspects of Closure of Atrial Septal Defects by the Atrioseptopexy Technic**
J. DICKENS, H. GOLDBERG, and D. F. DOWNING. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 1088–1110, June, 1956. 4 figs., 7 refs.

This paper from Hahnemann Medical College, Philadelphia, presents the clinical and physiological findings in 50 patients aged 5 to 51 years before and after the closure of an atrial septal defect, and the later results in 29 of these who were studied postoperatively over periods ranging from 3 months to 2½ years. Before operation the most common complaints were dyspnoea (46 cases) and decrease in exercise tolerance (44 cases). Cardiac catheterization, which was performed in 45 cases, showed that pulmonary hypertension was present in 33, being marked in 20 cases. The operation (atrioseptopexy) consisted in suturing the right atrial wall to the edges of the defect, converting the atrial cavity into the shape of a doughnut. In all, 13 patients died during or soon after operation. Postoperative arrhythmias occurred in 20 patients and congestive failure in 9. No features of the preoperative examination were found helpful in forecasting which patients might develop congestive failure, but the authors suggest that occasionally the proximity of the defect to the orifice of the superior or inferior vena cava may result in some compromise of these orifices in the attempt to obtain complete closure by this method.

Of the 29 patients studied postoperatively, clinical improvement occurred in all but 3. Cardiac catheterization studies carried out in 24 cases showed that the intracardiac shunt had been eliminated in 22. In 8 out of 12 cases in which pulmonary hypertension was present before operation the pressure returned to within normal limits. Exercise tolerance increased in all patients in whom the intracardiac shunt was abolished, and symptoms disappeared in all but 4 of these. With closure of the defect and return of the pulmonary blood flow to within normal limits there was a decrease in heart size in 24 (80%), and the preoperative cardiac murmurs disappeared in many cases. It is suggested that the systolic murmurs heard in these patients are due to an increased rate of blood flow through a normal pulmonary valve into a dilated artery.

R. G. Rushworth

CHRONIC VALVULAR DISEASE

1471. **Abnormal Ventilatory Patterns in Mitral Stenosis**
R. S. COSBY, E. C. STOWELL, W. R. HARTWIG, and M. MAYO. *Diseases of the Chest* [*Dis. Chest*] **29**, 633–640, June, 1956. 10 refs.

Cardiac catheterization and respiratory function tests were carried out at the University of Southern California School of Medicine and the County Hospital, Los Angeles, on 61 patients with pure mitral stenosis. The patients were divided into four groups according to the mean pulmonary arterial pressure. Those in whom this pressure was highest (Group 1) were in heart failure at the time of examination or gave a history of heart failure. With decreasing pulmonary arterial pressure in Groups 1, 2, and 3, there was a gradual increase in cardiac output, a decrease in pulmonary vascular resistance, and a rise in arterial oxygen saturation. Only in Group 1 did the mean arterial oxygen saturation fall below 90%. The mean vital capacity was below normal in all groups.

The degree of dyspnoea was more closely related to the height of the pulmonary arterial pressure and to vital capacity than to maximum breathing capacity; there was no relationship, however, between the degree of dyspnoea and arterial oxygen saturation. No striking correlation was observed between the cardiac defect and the respiratory abnormality, correlation being closest between vital capacity and the mean pulmonary arterial pressure. Anomalous values for the cardiac output and respiratory measurements were obtained in some of the patients with the lowest pulmonary arterial pressure (Group 4), and it is suggested that these patients may

have had subclinical left ventricular failure, presumably related to rheumatic myocarditis.

The significance of abnormalities of distribution and diffusion is discussed, with 3 illustrative cases.

T. Semple

1472. **Effect of Mitral Valvotomy on Renal Function**
J. HAMMOND, J. MACKINNON, and W. WHITAKER. *British Medical Journal* [*Brit. med. J.*] **2**, 71–73, July 14, 1956. 12 refs.

It has been suggested that the abnormal renal circulation which exists in patients with chronic rheumatic heart disease, such as mitral stenosis, is responsible for the impaired salt and water excretion in these patients and for the subsequent development of heart failure. In an attempt to account for the remarkable amelioration sometimes seen in such cases after operation the authors have investigated the renal function in one male and 14 female patients at the Royal Hospital, Sheffield, before and after mitral valvotomy. The clinical state was assessed according to the five grades (0–4) of Baker *et al.* (*Brit. med. J.*, 1952, **1**, 1043; *Abstracts of World Medicine*, 1952, **12**, 418) which range from "no disability" to "total incapacity", and the renal plasma flow (by sodium PAH clearance) and glomerular filtration rate (by inulin clearance) determined before and after operation in all cases. In 5 cases the diuretic response to ingested water was also tested. The detailed results of these investigations are tabulated.

Twelve months after operation one of the patients had died, one was clinically unchanged, but the clinical state of the 13 others had improved by one or two grades although none had reached Grade 0 (no disability). The renal function had improved markedly in one case and less markedly in 4 others, was further reduced in 4 cases, and showed little change in the remainder. In 3 of the 5 patients tested the diuretic response was improved. The authors suggest that these results indicate the need for further study of this problem.

David Friedberg

1473. **The Postcommissurotomy Syndrome**
C. PAPP and M. M. ZION. *British Heart Journal* [*Brit. Heart J.*] **18**, 153–165, April, 1956. 9 figs., 18 refs.

The term "postcommissurotomy syndrome" was first used by Soloff *et al.* (*Circulation* (*N.Y.*), 1953, **8**, 481; *Abstracts of World Medicine*, 1954, **15**, 401). In this paper from the London Chest Hospital the authors describe the syndrome as seen in 22 out of 100 patients after the performance of mitral valvotomy. The characteristic signs were fever, pericarditis, left pleural effusion, and a tendency to relapse. In 14 of the cases (Group I) the syndrome developed between the 8th and 34th postoperative days, while in the other 8 (Group II) it did not occur until 4 weeks to 4 months after operation. Fever was always moderate and was of shorter duration in Group II. The diagnosis of pericarditis was made on electrocardiographic evidence in 15 patients and the presence of a pericardial rub in 11 patients; pain was noted by only 6 of the patients. Left pleural effusion, which was blood-stained in 10 out of 11 cases, often persisted for many weeks and tended to recur after thoracentesis. Bacteriological culture was sterile in all but one case. Relapses, which resembled the initial syndrome, usually occurred 3 to 10 weeks after the original attack.

A study of the entire series of 100 patients revealed that fever lasting for a few days, left pleural effusion, and transient signs of pericarditis were observed in the majority, even in the absence of the full syndrome. From this it is concluded that the postcommissurotomy syndrome represents an accentuation and prolongation of the usual post-valvotomy sequelae and is probably due to postoperative oozing of blood from the left atrial wound. Loculated pleural effusion and consolidation at the base of the left lung may be additional causes. The absence of arthritis, carditis, and any definite response to the administration of salicylates argue against the syndrome being due to postoperative recurrence of rheumatic activity. Treatment is non-specific, and the prognosis is good.

[The fact that this syndrome has also been observed after intracardiac operations for congenital heart disease suggests that the term "postcardiotomy syndrome" would be more appropriate.] *Gerald R. Graham*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1474. **Evaluation of the Serum Glutamic Oxalacetic Aminopherase (Transaminase) Test. Its Use in Diagnosis of Acute Myocardial Infarction**
J. L. DENNEY, C. B. MCAULEY, H. E. MARTIN, A. G. WARE, and M. SEGALOVE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 614–616, June 16, 1956. 8 refs.

At Los Angeles County Hospital the serum glutamic oxalacetic aminopherase (transaminase) level was determined in 95 patients with definite or suspected myocardial infarction and compared with that in 55 patients with other diseases. The estimations were carried out daily for 5 days in the majority of cases, and a mean serum transaminase level above 40 units was considered to be abnormal.

Of the 77 cases of unequivocal myocardial infarction, the level was above normal in 63 and normal in 14 cases; of the latter, however, 11 were considered to have been inadequately studied and the authors conclude that only 3 cases gave false negative results. Of 18 cases of suspected myocardial infarction, the serum aminopherase level was above normal in 12; but no conclusions could be drawn from this finding under the conditions of the investigation.

Of 35 cases of cardiovascular diseases other than myocardial infarction, the level was high in 8, these including 2 cases of angina pectoris and 2 of pulmonary embolism. However, in 2 other cases of pulmonary embolism the levels were within normal limits. Of 20 varied cases of disease not involving the cardiovascular system, the serum aminopherase level was raised in 12, namely, 5 cases of hepatic disease, 2 of complicated

diabetes, and 5 of haemorrhagic pancreatitis; but in 5 other cases of pancreatitis the levels were found to be normal.

The authors conclude that elevation of the serum aminopherase level is highly suggestive of myocardial necrosis, provided that other types of tissue necrosis, hepatic disease, and jaundice can be excluded. The height of the serum aminopherase level is in rough correlation with the severity of the infarction. It is recommended that the serial determinations should be begun as soon as possible after the infarction, as the rise in the serum transaminase level may be transient; in 88% of the present cases the highest level was observed on the second day.

The rise in the aminopherase level in only half the cases of pulmonary embolism and of acute pancreatitis appears to limit the usefulness of the test in the differential diagnosis of conditions other than myocardial infarction.

Marcel Malden

1475. **Results of Treatment of Angina Pectoris with Choline Theophyllinate by the Double-blind Method**

C. ARAVANIS and A. A. LUISADA. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 1111–1122, June, 1956. 2 figs., 13 refs.

A trial of choline theophyllinate in the treatment of angina of effort is reported from the Mount Sinai Hospital, Chicago, and the Chicago Medical School. The double-blind technique was used, 42 patients receiving the drug while 28 others received a placebo. The results were assessed by means of clinical and electrocardiographic records. The drug produced definite clinical improvement in 52·3% of cases after 2 to 4 weeks, with a decrease in the number of attacks of pain and in their severity, and an increase in working capacity and ability to walk without pain. There was little change in the electrocardiographic findings at rest, but in those cases in which the effects of comparable degrees of exertion were recorded before and after treatment the latter tracing showed much less deterioration after exercise. The possible mechanism of action of the drug is discussed, but no conclusion is reached. The dose given was 200 mg. 3 times daily, for one month in most cases and for 4 to 12 months in a few.

J. B. Wilson

1476. **Anticoagulant Treatment in Acute Coronary Occlusion with Special Reference to Indications.** [In English]

C. HOLTEN. *Acta medica Scandinavica* [*Acta med. scand.*] **155**, 15–25, June 30, 1956. 10 refs.

The author presents the case for the early treatment with anticoagulants of all cases of myocardial infarction (with certain specific exceptions), considering it misleading to attempt to distinguish between "poor-risk" and "good-risk" cases within 24 hours of admission, as proposed by Russek and Zohman (*Amer. J. med. Sci.*, 1952, **224**, 496; *Abstracts of World Medicine*, 1953, **14**, 40); among 200 consecutive cases of coronary occlusion admitted to the Municipal Hospital, Aarhus, Denmark, during the period 1951–4, arrhythmia (other than extrasystoles) or congestive failure was present within the first 24 hours in 38, but one or both of these grave signs developed later in a further 44 cases. He suggests that the lessened coagulability of the blood not only reduces the spread of coronary thrombosis if present, the risk of thrombosis in peripheral vessels, and the potential danger of the formation of thrombi in the heart after the 5th day, but also directly influences the occlusive process in the coronary arteries. In support of this he points out that anticoagulant treatment reduces mortality in the first week after coronary infarction to a significantly greater degree than it reduces the incidence of thrombo-embolic incidents.

Owing to the slowness of effect of coumarin derivatives heparin must be used if the coagulability of the blood is to be reduced without delay. This usually necessitates repeated intravenous injections during the first 48 hours, until dicoumarol begins to take effect, but a suitable colloid solution for intramuscular injection has been developed by the author which contains 1·25% of carboxymethylcellulose and 10,000 units of heparin per ml., 2 ml. given intramuscularly increasing the coagulation time to 30 minutes within 2 hours and the effect lasting for 8 hours. Since February, 1955, some 300 injections of this preparation have been given to 60 patients, without local reactions. To a patient of average weight an initial dose of 2 ml. is given, followed by 5 doses of 1 ml. at 8-hourly intervals. The coagulation time is determined immediately before each injection. During 3 years 166 cases of acute coronary occlusion have been treated with heparin and dicoumarol, with 43 deaths; slight haemorrhage occurred in 5 cases and there were 5 cases of thrombo-embolic complications, all occurring either before the anticoagulant treatment had become effective or after it had been discontinued.

The author suggests that with correct administration, adequate dosage, and constant laboratory control anticoagulants may be used with benefit and without fear of complications in the treatment of ischaemic heart disease.

V. Reade

BLOOD VESSELS

1477. **Coarctation of the Aorta**

W. P. CLELAND, T. B. COUNIHAN, J. F. GOODWIN, and R. E. STEINER. *British Medical Journal* [*Brit. med. J.*] **2**, 379–390, Aug. 18, 1956. 10 figs., 31 refs.

The authors have studied, at Hammersmith Hospital (Postgraduate Medical School of London), 52 patients (34 male and 18 female) who were suffering from coarctation of the aorta, in 40 of whom resection was carried out. Of these cases, 43 were discovered accidentally as there were virtually no symptoms. The authors are of the opinion that many of the symptoms which develop after diagnosis are due to a cardiac anxiety state. In 8 cases vegetations were present at the site of the stenosis, but in only one of these was a diagnosis of endarteritis made before operation. The series included 2 cases of dissecting aneurysm and 2 of saccular aneurysm, and there were 3 cases of cerebral vascular

accident. All the patients had hypertension. The causes of death and the natural history of the disease are discussed.

Of the 40 patients undergoing resection, 3 died as a direct result of the operation, but in the remainder, who have been followed up for varying periods up to 8 years, the results have been excellent. The average decrease in blood pressure was 32 mm. Hg systolic and 16 mm. Hg diastolic. It was noted that a return to a completely normal blood pressure was more common in the younger age groups. *J. R. Belcher*

1478. **Surgical Treatment of Children with Coarctation of the Aorta**
A. L. D'Abreu and C. Parsons. *British Medical Journal* [*Brit. med. J.*] **2**, 390–393, Aug. 18, 1956. 5 figs., 3 refs.

In discussing the selection of patients for operation and the probable prognosis in coarctation of the aorta in children, the authors report that during a 5-year period at the Children's Hospital, Birmingham, 30 infants died as a result of aortic coarctation, whereas during the same period there were no deaths from this cause in children between the ages of 6 months and 14 years. Most (25) of the infants who died did so within the first month of life and had the infantile type of stenosis. Comparison with three post-mortem series reported in the literature suggests that if children with coarctation survive their first year they are unlikely to die before the age of 10, but their chance of survival over the age of 40 is poor.

The diagnosis and the operative technique are briefly discussed. The results in 10 children who were treated by resection were good in all except one, in whom cardiac deterioration had taken place before operation was decided on. One child died as the result of operation, and 2 patients later developed a new stricture. A progressive decrease in the blood pressure was the rule, although it took several weeks to reach its new level. In the authors' opinion the best time for operation is between the ages of 5 and 10 years. *J. R. Belcher*

1479. **An Evaluation of Peripheral Arteriosclerotic Insufficiency Utilizing Radioactive Iodinated Human Serum Albumin**
E. J. Halligan, J. C. Gibbs, R. V. Grieco, and J. E. McKeown. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 511–516, May, 1956. 6 figs., 8 refs.

A preliminary study is reported of the use of human serum albumin containing tracer amounts of radioactive iodine and injected into the antecubital vein for the purpose of studying the peripheral circulation by determining the radioactivity at various points with a scintillation counter. From the results obtained in 75 patients with varying degrees of arterial insufficiency in the legs the authors confirm the finding of Krieger *et al.* (*Ann. Surg.*, 1952, **136**, 357; *Abstracts of World Medicine*, 1953, **13**, 219) that this method is more accurate than any other at present available for the evaluation of the peripheral circulation. The method is simple and safe, can be repeated, and is useful for diagnostic as well as prognostic purposes. It may be of value in assessing the reserve vascular bed and the effects of different forms of treatment, such as intra-arterial injections or lumbar sympathectomy.

The authors have been unable to detect any consistent improvement in circulation after lumbar sympathectomy in patients with advanced disease, and they conclude that sympathectomy should be limited to those patients with moderate arteriosclerosis, embolism, and vasospastic conditions. *Leon Gillis*

1480. **The Prognosis of Patients with Intermittent Claudication**
W. B. Spaulding. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **75**, 105–111, July 15, 1956. 6 refs.

1481. **The Principles of the Prophylaxis and Treatment of Atherosclerosis.** (Принципы предупреждения и лечения атеросклероза)
B. V. Il'inskiĭ. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 19–27, No. 5, May, 1956.

According to Anichkov and his co-workers atherosclerosis is not a physiological process but a disease. They have shown that 5 to 10% of persons dying in old age show no sign of it, while a considerable number dying at 35 to 40 or even younger have been found to suffer from it. Moreover, it has been proved that atheromatous changes in their earlier stages are reversible —although it is true that treatment has to be of long duration. Once the fourth decade is reached, however, atheroma progresses swiftly to a point at which it is irreversible, while the dangers inherent in the disease are liable to be of sudden onset.

In the present author's view the aetiological factors can be divided into: (1) predisposing, (2) provocative, and (3) aggravating. Among the first are a hereditary predisposition to nervous, metabolic, and vascular or endocrine disease, sex (atheroma is much commoner in males), and age. Provocative factors include external or internal conditions leading to disturbances of metabolism, especially of cholesterol metabolism; undoubtedly the cerebral cortex and higher nervous centres play an important part in such disturbances. Aggravating factors include hypertension, dystrophic changes in the arterial walls, endocrine dysfunction (especially hypothyroidism), toxic effects of nicotine, lead, alcohol, carbon disulphide, and sulphuretted hydrogen (in the manufacture of viscose), and other industrial hazards, including abrupt changes in temperature such as occur in deep coal mines. The prophylaxis of atheroma is thus similar to that of hypertension, chronic nephritis, myxoedema, diabetes mellitus, and other metabolic disorders.

In the absence of any specific medication, prophylactic treatment is primarily by diet and improvement of the environment. The general dietetic principles are: (1) adaptation of the diet to age, nature of occupation, and pattern of life (especially the avoidance of overeating); (2) strict limitation of foods rich in cholesterol, animal fats, and vitamin D, and of easily assimilated

carbohydrates; (3) a greater proportion of foods rich in lipotropic substances, such as choline (contained in junket, herring, cod, and yeast), tyrosine, tryptophane, and methionine (contained in milk), glycocol (found in beetroot juice and molasses), lecithin (present in soya bean), and ascorbic acid. Poorly assimilated carbohydrates, such as nuts, haricot beans, turnip, and cabbage, are valuable (if well tolerated) in that they assist in the elimination of cholesterol. A basic diet suggested for patients with evidence of disturbed cholesterol metabolism would be as follows: fat (mainly of vegetable origin) 25 g.; protein 80 to 100 g.; and carbohydrate 430 to 470 g.

Equally important is the social adjustment of persons subject to mental, emotional, and environmental strains. As far as possible these should be abolished, and regular alternation of physical exercise, brain work, and rest should be arranged; toxic hazards should be reduced to the minimum, diseases such as chronic nephritis or hypothyroidism should be treated, and the blood cholesterol content should be estimated at intervals. Such a regimen involves the setting up of special clinics and dispensaries at which adequate pathological laboratory services must be available. Early recognition before symptoms appear is important, and therefore the determination of the blood content of cholesterol should be as much a routine procedure as of that, for example, of sugar. The author concludes that for dealing with such a widely distributed disease as atherosclerosis a large-scale organization is required.

L. Firman-Edwards

HYPERTENSION

1482. **Human Arterial Hypertension: a State of Mild Chronic Hyperaldosteronism?**

J. GENEST, G. LEMIEUX, A. DAVIGNON, E. KOIW, W. NOWACZYNSKI, and P. STEYERMARK. *Science* [*Science*] **123**, 503–505, March 23, 1956. 1 fig., 8 refs.

At the Hôtel-Dieu Hospital, Montreal, the authors determined the aldosterone content of urine from 6 patients with malignant hypertension, 7 patients with severe essential hypertension, and 5 adult male control subjects. The criteria adopted for the diagnosis of malignant hypertension were papilloedema, diastolic pressure over 130 mm. Hg, diminished renal function, and poor general condition. The cases of essential hypertension all showed fundal exudates and haemorrhages and signs of severe left ventricular strain.

Each 24-hour collection of urine was adjusted to *p*H 1 and extracted four times with chloroform. The urine was then re-adjusted to *p*H 4·5, incubated for 24 hours with β-glucuronidase, and re-extracted. The combined extracts were washed with 0·1 N sodium hydroxide solution and with water and evaporated to dryness, and chromatography was then carried out on toluene–propylene glycol. The aldosterone–cortisone zone was subjected to further chromatography in the Bush C system and the aldosterone zone eluted for bioassay in rats. Each test animal was injected with a 20-minute or 40-minute aliquot of the 24-hour urine extract. Other rats each received 0·2 or 0·4 μg. of aldosterone, or 0·1 ml. of ethanol as a control.

No significant difference was found between the three groups when the 20-minute aliquots were tested. The 40-minute aliquots, however, did show a significantly higher urinary aldosterone excretion in the two hypertensive groups compared with the controls. It is suggested that human arterial hypertension might be caused by mild chronic hyperaldosteronism.

Denis Abelson

1483. **The Relation of Angiotonin and L-Norepinephrine to Essential Hypertension as Determined by the Reaction of the Nailfold Capillary Bed**

S. E. GREISMAN. *Journal of Experimental Medicine* [*J. exp. Med.*] **103**, 477–486, April 1, 1956. 3 figs., 16 refs.

The response of the cutaneous arteriolar bed to the intravenous infusion of L-noradrenaline and angiotonin (hypertensin) was studied at Bellevue Hospital, New York, by observing microscopically the nail-fold capillary vessels in 11 patients without demonstrable cardiovascular disease and in one with generalized arteriosclerosis.

The infusion of noradrenaline in a concentration of 4 μg. per ml. at progressively increasing rates produced sustained ischaemia of the capillary bed even before elevation of the diastolic arterial blood pressure to hypertensive levels occurred. In contrast, angiotonin in a 4% solution did not produce nail-fold ischaemia, even when hypertensive diastolic arterial blood pressure levels had been reached. Comparison of the nail-fold capillary bed of one subject with angiotonin-induced hypertension with that of a patient with essential hypertension showed that they were microscopically indistinguishable. The infusion of angiotonin into subjects without cardiovascular disease increased the reactivity of the capillary bed to circulating noradrenaline to a level similar to that in patients with essential hypertension.

It is concluded from its effects on the nail-fold capillaries that angiotonin, but not noradrenaline, acts like the hypothetical humoral pressor substance thought to cause essential hypertension, that is, it constricts the arteriolar bed and so increases total systemic peripheral resistance without, however, reducing cutaneous blood flow.

Gerald R. Graham

1484. **Two New Ganglion-blocking Agents in Treatment of Hypertension**

S. LOCKET. *British Medical Journal* [*Brit. med. J.*] **2**, 116–122, July 21, 1956. 1 ref.

From Oldchurch Hospital, Romford, Essex, are described the effects of two new quaternary ammonium compounds in the treatment of hypertension. They resemble other quaternary ammonium compounds in general use in being ganglion-blocking agents, but differ from them principally in their longer duration of action. The drugs are referred to by their laboratory reference numbers 356c54 and 139c55, the former being N^1:N^1:N^2-trimethyl-N^1-(6-cyano-6:6-diphenylhexyl)ethylene-1-

ammonium-2-morpholinium dichloride and the latter is a lower homologue.

For clinical use the dose of 356c54 given intravenously was 2 to 12 mg., given subcutaneously it was 10 to 40 mg., and given by mouth about 12 to 15 times the subcutaneous dose. The effective dose of 139c55 was about half that of 356c54. The effect of both drugs was delayed—5 to 25 minutes when given intravenously and 10 to 60 minutes when given subcutaneously, though blurring of vision, often accompanied by bradycardia, usually appeared within a few minutes of either intravenous or subcutaneous injection. The blood pressure began to fall within another 10 minutes, the maximum fall being reached 45 to 60 minutes later. The duration of action exceeded that of hexamethonium or pentolinium, the effect lasting at least 9 hours and sometimes longer than 24 hours.

Details are given of the effects of these two drugs given subcutaneously to 15 patients suffering from hypertension, the majority of whom had previously received treatment with other drugs. The author states that the results were most satisfactory, the drugs having the advantages of a more gradual onset and greater duration of action, and lack of effect on the small intestine.

[Further clinical trials are needed to assess the value of these interesting new ganglion-blocking compounds compared with other hypotensive drugs.]

R. Wien

1485. **The Effect of a Ganglionic Blocking Agent (Hexamethonium) on Renal Function and on Excretion of Water and Electrolytes in Hypertension and in Congestive Heart Failure**

T. D. Ullmann and J. Menczel. *American Heart Journal* [*Amer. Heart J.*] **52**, 106–120, July, 1956. 4 figs., 33 refs.

1486. **A Long-term Study of the Effects of Crude Rauwolfia Serpentina and of its Alseroxylon Fraction in Patients with Hypertension**

R. S. Green and D. Davolos. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 760–773, May, 1956. 1 fig., 13 refs.

Crude extract of *Rauwolfia serpentina* or its alseroxylon fraction (" rauwiloid ") was tried at St. Mary's Hospital, Cincinnati, Ohio, in the treatment of 40 patients with well-established hypertension; of these, 36 were suffering from cardiac, renal, or cerebral damage, the other 4 being relatively young patients with persistently high diastolic pressure but without detectable complications. The effect was judged from the average systolic, diastolic, and mean arterial pressures for the entire period, for each week, and also for each 4-week period during therapy. Mean arterial pressure was calculated by adding one-third of the pulse pressure to the diastolic pressure. The period of treatment varied from 15 to 89 weeks.

A reduction of more than 10 mm. Hg in the average mean arterial pressure occurred in 18 cases, while an average diastolic pressure of less than 90 mm. Hg was achieved in 13 (32·5%) of the patients, this result being obtained, on the average, at the end of 14 weeks (range 4 to 36 weeks). The hypotensive action of the drug was not influenced by the severity of the hypertension or the associated complications. Furthermore, the beneficial effect of the drug was not limited to its hypotensive action, for definite improvement of complications was noted in patients with angina, coronary insufficiency, recent myocardial infarction, cerebrovascular accident, hypertensive cardiovascular disease, and congestive heart failure. Two patients with chronic uraemia also responded favourably. The usual side-effects were encountered and necessitated reduction in the dosage, while 7 patients made the unusual complaint of nightmares, which disappeared promptly on withdrawal of the drug. Transient episodes of peripheral neuritis and a tendency to amenorrhoea in younger females were noted. It is suggested that a course of 6 mg. daily for 12 weeks is adequate to determine whether or not a fall in blood pressure will be produced by rauwiloid alone. The total daily dose is best administered at bedtime. Doses larger than 4 to 6 mg. of rauwiloid are not necessary since they do not increase the hypotensive action. The maintenance dose may be as low as 1 mg. daily or less, but the optimum level is usually about 4 mg. daily.

A. I. Suchett-Kaye

1487. **Results of Prolonged Treatment with Pentolinium Tartrate with Special Reference to the Addition of Rauwolfia, Hydralazine or Both**

E. D. Freis and I. M. Wilson. *Circulation* [*Circulation (N.Y.)*] **13**, 856–865, June, 1956. 3 figs., 16 refs.

This paper from Georgetown University School of Medicine, Washington, D.C., reports the authors' experience in treating 96 patients " selected because of severe, sustained hypertension " with pentolinium tartrate, either alone or together with other hypotensive agents, for periods ranging from 3 to 27 (average 12) months. The average age of the patients was 47 (range 27 to 65), 71 of them were male and 25 female, and 54 (56%) had retinopathy of Grades III or IV. Cardiac enlargement was present in 58 out of 76 of the patients examined radiologically. At various times and for various periods 54 of the patients received pentolinium tartrate (P.T.) alone [presumably by injection], 71 received P.T. plus rauwolfia, 20 P.T. plus hydrallazine, and 50 all three drugs together, the results in the various treatment groups being then compared; details of the reductions in blood pressure in each group are given.

Most of the patients derived some benefit from the treatment. The most marked improvement was in the optic fundal appearances, 80% of the patients with retinopathy of Grades III and IV showing improvement. The authors conclude that a smaller dosage of pentolinium was required to produce an adequate reduction in blood pressure when either of the adjuvant drugs was added, and that a combination of all three agents resulted in the greatest fall in blood pressure combined with the fewest side-effects arising from ganglionic blocking.

[This paper simply confirms, on a very heterogeneous sample of cases, conclusions already established in this field. An average period of treatment of 12 months hardly seems to justify the use of the term " prolonged " in the title.]

P. Hugh-Jones

Haematology

1488. **Radioactive Iron Studies in Routine Haematological Practice**
G. WETHERLEY-MEIN, M. S. R. HUTT, W. A. LANGMEAD, and M. J. HILL. *British Medical Journal* [*Brit. med. J.*] **1**, 1445–1449, June 23, 1956. 8 figs., 13 refs.

The authors of this communication from St. Thomas's Hospital, London, review current techniques involving the use of radioactive iron (^{59}Fe) in the study of human metabolism and haematological disorders. The plasma clearance and erythrocyte utilization of injected ^{59}Fe (as ferric chloride) have been determined in a study of 70 patients with leukaemia and various types of anaemia. Radioactivity in the blood samples was measured by means of a well-type scintillation counter, and external counting rates over the heart, bone marrow (sacrum), liver, and spleen determined by the technique described by Ledlie and Baxter. The radiation hazard from 10 μc. of ^{59}Fe given intravenously is stated to be negligible to the patient.

The behaviour of the iron metabolic pattern was studied in detail by these methods in some 15 different disorders. The authors suggest that although the use of radioactive iron may not be essential for haematological diagnosis the method provides the only readily available laboratory technique by which the dynamics of erythropoiesis can be studied, conditions such as aplasia of bone marrow or haemolytic anaemia being particularly suitable for diagnosis by these methods. [This is an excellent review of the subject.] *I. McLean Baird*

1489. **Thrombocytopenic Purpura Due to Quinidine. I. Clinical Studies**
F. G. BOLTON and W. DAMESHEK. *Blood* [*Blood*] **11**, 527–546, June, 1956. 35 refs.

Cases of thrombocytopenia resulting from the administration of drugs include a group in which a hypersensitivity reaction is responsible, and in which it is likely that the drug, acting as a hapten to the platelet, confers antigenicity on it. An antibody then develops against the platelet–drug antigen. In this paper from Tufts University School of Medicine, Boston, 5 cases of this type of thrombocytopenic purpura due to quinidine are described in detail. The patients were one man and 4 women who had been taking quinidine for various periods. In each of these cases an antibody was demonstrated in the patient's plasma, capable of agglutinating platelets *in vitro* in the presence of quinidine.

The authors present in tabular form details of 23 previous similar cases reported in the literature. The condition is most frequent in women over 50 years of age. It is an acute self-limiting disease and the prognosis is good if quinidine therapy is stopped early in the course of the condition, recovery usually taking place within 3 to 14 days after withdrawal of the drug. The onset of the purpura may occur after varying periods of administration of quinidine, but follows quickly after the causative dose. The authors stress that intra-oral haemorrhagic bullous lesions are very suggestive of a thrombocytopenia of this type due to a drug.

A. S. Douglas

1490. **Thrombocytopenic Purpura Due to Quinidine. II. Serologic Mechanisms**
F. G. BOLTON. *Blood* [*Blood*] **11**, 547–564, June, 1956. 15 refs.

In this paper the author describes the serological investigations carried out in one of the cases of quinidine thrombocytopenia described above [Abstract 1489]. The author compares his results with those of Ackroyd (*Clin. Sci.*, 1954, **13**, 409; *Abstracts of World Medicine*, 1955, **17**, 384) whose work on thrombocytopenia due to "sedormid" has stimulated recent interest in this type of drug thrombocytopenia. [For full technical details of the present author's careful experiments the original paper should be consulted.]

He showed that in the presence of quinidine the antibody in the patient's blood caused platelet agglutination, but that this did not happen in the presence of quinine, a stereo-isomer of quinidine. Lysis of platelets was demonstrated in the presence of complement, and the platelet–drug antibody fixed complement. Platelets exposed to quinidine and the antibody could then be separated and shown to fix complement; the platelets in the presence of quinidine were apparently able to adsorb antibody. No union could be demonstrated between the platelets and quinidine or between the antibody in the patient's plasma and quinidine. Dialysis of the platelet–quinidine–antibody complex against saline resulted in its splitting into its three constituents. It was shown that the antibody in the patient's plasma was contained in the gamma-globulin fraction. Since platelets and blood vessels may be antigenically similar the author incubated together macerated choroid plexus, quinidine, and the patient's serum, but no complement-fixation was demonstrated. The antibody is thought, therefore, to be inactive against blood vessels.

A. S. Douglas

1491. **Hemophilia: Quantitative Studies of the Coagulation Defect. A Modified Prothrombin-consumption Test Using Erythrocytin**
A. J. QUICK and C. V. HUSSEY. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 524–531, May, 1956. 1 fig., 14 refs.

Haemophilia, which is due to a deficiency of antihaemophilic globulin (thromboplastinogen), occurs in various clinical grades of severity, according to the degree of the deficiency. This paper from Marquette University School of Medicine, Milwaukee, describes a method for the quantitative assay of antihaemophilic globulin based on the prothrombin consumption test

modified by the addition of an extract of haemolysed erythrocytes. This extract contains a factor (called "erythrocytin" by the authors) which will replace platelets in the clotting system and is much more potent, so that with an excess of erythrocytin a direct relation can be demonstrated between the concentration of thromboplastinogen and the prothrombin consumption time. The assay is performed with plasma from a severe case of haemophilia in which the quantity of thromboplastinogen can be regarded as negligible, to which varying amounts of fresh normal plasma are first added and the prothrombin consumption time determined for each, the values being plotted against the amounts of plasma added to give a straight-line graph. The test is then repeated with a fixed quantity of the plasma to be tested in place of the normal plasma, its content of thromboplastinogen in relation to that of normal plasma being determined by reference to the graph.

The authors found that in a mild case of haemophilia the plasma thromboplastinogen concentration determined by this method was 0·5 to 1% of normal, in a moderate case about 0·5%, and in a severe case too small to be measured. The degree of the haemophilic defect appears to be transmitted quantitatively, the severity of the disease being the same in all the affected members of a family.

Determination of the plasma thromboplastinogen content in severe haemophiliacs after a transfusion of fresh blood or plasma showed that although the thromboplastinogen disappears fairly rapidly from the blood, the level remains at 0·5% of normal or higher 24 hours after a transfusion of 500 ml. in an adult.

[The levels of antihaemophilic globulin in the various grades of haemophilia recorded in this paper are considerably lower than those reported by other investigators.] *A. S. Douglas*

1492. **Pseudohemophilia Type B. Hereditary Hemorrhagic Diathesis Characterized by Prolonged Bleeding Time and Decrease in Antihemophilic Factor**
K. Singer and B. Ramot. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 715–725, June, 1956. 1 fig., 45 refs.

The authors describe, from the Michael Reese Hospital, Chicago, a case of hereditary haemorrhagic diathesis in a 13-year-old girl, the offspring of a cousin intermarriage. There had been an older brother who had died, and he also had a serious haemorrhagic tendency, but otherwise the family history was negative.

Laboratory investigation in this case showed that the patient's bleeding time was prolonged in the presence of a normal platelet count. There was, in addition, evidence of a blood thromboplastin defect, the prothrombin consumption being defective. It was subsequently established that this defect was due to a deficiency of antihaemophilic globulin by demonstrating the failure of the patient's adsorbed plasma to correct haemophilic adsorbed plasma in the thromboplastin generation test, and its failure to correct the defective prothrombin consumption of haemophilic blood. The concentration of antihaemophilic globulin in this case was estimated to be between 19 and 22% of normal. Other aspects of the coagulation mechanism were normal. No thromboplastin defect was found in the patient's platelets by means of the thromboplastin generation technique.

The authors present a careful review of 19 similar cases of prolongation of the bleeding time associated with deficiency of antihaemophilic globulin reported in the literature. They propose to name the condition "pseudohaemophilia Type B", and discuss the differences between this type of haemorrhagic disease, with prolongation of the bleeding time, and other varieties of vascular pseudohaemophilia. The genetic aspects of this dual type of defect are also considered. It is thought likely that pseudohaemophilia B may be transmitted by autosomal genes behaving either as Mendelian dominants or as recessives. *A. S. Douglas*

1493. **Neurological Complications of Haemophilia and Christmas Disease**
A. S. Douglas and S. G. McAlpine. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 270–273, Aug., 1956. 3 refs.

1494. **Amino-aciduria in the Megaloblastic Anaemias**
K. J. Keeley and W. M. Politzer. *Journal of Clinical Pathology* [*J. clin. Path.*] **9**, 142–143, May, 1956. 3 refs.

In a study carried out at Baragwanath Hospital, South Africa, the authors, using one-dimensional chromatography, have confirmed the presence of amino-aciduria in one case of untreated Addisonian pernicious anaemia in a European. One male African patient with pernicious anaemia showed a similar urinary amino-acid pattern before treatment with cyanocobalamin, but no excess of amino-acids was detectable in the urine afterwards; the authors point out, however, that there has been no fully substantiated case of Addisonian pernicious anaemia in an African. In none of 12 cases of non-Addisonian megaloblastic anaemia in African women (7 post partum) and 2 of nutritional megaloblastic anaemia in infants was amino-aciduria found. The authors suggest that urinary chromatography might prove to be a simple method of differentiating Addisonian from other megaloblastic anaemias. *R. B. Thompson*

1495. **The Treatment of Polycythaemia Vera with "Daraprim" [Pyrimethamine].** (Behandlung der Polycythaemia vera mit Daraprim)
H. Kleinfelder and H. Bracharz. *Klinische Wochenschrift* [*Klin. Wschr.*] **34**, 512–516, May 15, 1956. 2 figs., 46 refs.

At the University Medical Clinic, Würzburg, one case of polycythaemia associated with myelosclerosis and 5 cases of polycythaemia vera were treated with "daraprim" (pyrimethamine), which is a folic acid antagonist. The haemoglobin value and erythrocyte count fell to normal levels in 2 to 3 months in response to doses of 50 mg. daily, smaller doses having proved ineffective. It is suggested, however, that too little is as yet known of the possible side-effects of this drug to justify its use in routine treatment. *A. Piney*

Respiratory System

1496. **The Mechanism of Cough Syncope**
H. D. McIntosh, E. H. Estes, and J. V. Warren. *American Heart Journal* [*Amer. Heart J.*] **52**, 70–82, July, 1956. 7 figs., 20 refs.

At Duke University School of Medicine, Durham, North Carolina, 13 patients suffering from cough syncope were studied with a view to eliciting the mechanism underlying this syndrome, simultaneous recordings of arterial, intrathoracic, and cerebrospinal pressure being obtained and the results compared with those in a group of 100 normal subjects. The response to coughing was qualitatively the same in both groups. The chief difference was that the patients with a history of cough syncope coughed more forcefully and longer than the normal subjects, producing on occasions increases in intrathoracic and cerebrospinal-fluid pressures approaching 300 mm. Hg [*sic*]. The rise in arterial pressure during a bout of coughing was significantly less than the rise in the intracavitary (intrathoracic and intracranial) pressures. It is suggested that the increased pressure in the cerebrospinal fluid, by increasing the extravascular pressure around the cranial arteries and veins, causes blood to be "squeezed" from the cranium, and that thus the blood supply to the brain is rapidly reduced, anoxia develops, and syncope may occur.

A. I. Suchett-Kaye

1497. **An Evaluation of Twenty-two Patients with Acute and Chronic Pulmonary Infection with Friedländer's Bacillus**
B. M. Limson, M. J. Romansky, and J. G. Shea. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 1070–1081, June, 1956. 10 refs.

This paper gives an account of 22 cases of pulmonary infection with Friedländer's bacillus which were admitted to the District of Columbia General Hospital (Georgetown University), Washington, over a period of 2½ years. Acute primary Friedländer's pneumonia was diagnosed in 13 cases, and 9 were cases of acute or chronic mixed pulmonary infection. All but one of the patients were male, and their ages ranged from 16 to 70, 11 being "in the older-age group"; 15 were alcoholics and 5 of these were in delirium tremens at the time of admission. The characteristic bloody and tenacious sputum associated with the disease was observed in half of the cases. Sputum culture was positive in all cases, and in 8 the blood culture was also positive. The leucocyte count varied from 1,000 to 30,000 per c.mm. Ten of the patients died—9 of the 13 with acute pneumonia and one of the 9 in the chronic group. Leucopenia was present in 8 of the fatal cases, a finding which thus appears to be of grave prognostic significance. All 9 patients with acute pneumonia who died were severely ill, and all were alcoholics, 4 of them in delirium tremens; 7 had positive blood cultures.

Delay in the initiation of treatment, or of treatment with the right drug, appeared to be an important factor contributing to a bad prognosis. A combination of streptomycin and one of the tetracycline group or chloramphenicol is regarded as the treatment of choice in acute Friedländer's pneumonia, and treatment should be initiated at once on the slightest suspicion of that condition. Cortisone was given to two patients, but both died.

Kenneth M. A. Perry

1498. **Abronchiectatic Bronchiectasis: the Recognition of Surgical Pneumonitis**
R. E. MacQuigg. *American Surgeon* [*Amer. Surg.*] **22**, 465–473, May, 1956. 8 figs., 4 refs.

From the Lovelace Clinic, Albuquerque, New Mexico, the author describes 2 cases of a syndrome which he terms "abronchiectatic bronchiectasis". One patient, a woman aged 57, had suffered from recurrent attacks of pneumonitis over a period of 3 years; resection of an emphysematous portion of her lung led to some temporary improvement. In the other case, also in a middle-aged woman, the results of bronchography were virtually normal, yet at operation the right middle lobe was found to be partially collapsed, and resection of the affected segment [not unnaturally] led to cessation of the previously recurrent respiratory infections.

[Unfortunately, these patients do not appear to have been adequately investigated; and the absence both of full clinical details and of reproductions of the relevant bronchograms makes any assessment of the results difficult.]

P. Mestitz

1499. **Pneumonia and Bronchopneumonia Treated with Sulphonamides and Antibiotics.** (Pneumonies et bronchopneumonies traitées par les sulfamides et les antibiotiques)
H. Durieu, F. De Clercq, A. De Coster, P. Golard, and M. Kunstler. *Acta clinica Belgica* [*Acta clin. belg.*] **11**, 105–131, March–April, 1956. 7 figs., 23 refs.

The authors review all cases of primary pneumonia and bronchopneumonia treated at the Hôpital Saint-Pierre (University Medical Clinic), Brussels, during the period 1931 to 1955.

There were 468 patients with lobar pneumonia, of whom 126 were treated with sulphonamides [not further specified], 165 with antibiotics (usually penicillin), and 177 expectantly only. A high mortality was related to advanced age, to the presence of pre-renal uraemia or to a leucocytosis above 15,000 per c.mm., and to delay in treatment. Of those treated with sulphonamides 20% died, of those treated with penicillin 5%, and of the remainder 30%. Although 13% of those receiving antibiotics were afebrile by the fourth day, compared with only 4% in the other groups, fever was still present 10 days after beginning treatment in about half the cases

in all three groups: nevertheless, the eventual outcome was usually good and it therefore seems inadvisable to abandon any particular form of chemotherapy because of an apparent lack of response. Penicillin was as successful in low dosage (200,000 to 400,000 units daily) as in high dosage. The incidence of purulent complications was least with penicillin.

There were 390 cases of bronchopneumonia, of which 35 were treated with sulphonamides, 102 with antibiotics, and 253 expectantly only. A poor prognosis was associated with the same factors as are mentioned above, though leucocytosis was of little significance, and both incidence and mortality were directly related to age. Mortality was 26% with sulphonamides, 15% with antibiotics, and 55% in the remainder. Fever and physical signs disappeared more rapidly with antibiotic treatment, but in contrast to lobar pneumonia the difference was most marked after 10 to 17 days. Penicillin in high dosage was particularly effective, but there were still a number of cases in which this antibiotic failed and streptomycin or one of the tetracycline group was substituted and produced a rapid response. [There is no bacteriological analysis of these last cases, in which it is possible that *Haemophilus influenzae* or resistant *Staphylococcus aureus* may have predominated; the frequency of such predominance is such, in the abstracter's opinion, as to justify treatment with a combination of penicillin and streptomycin from the start in all cases of bronchopneumonia.] The use of antibiotics decreased enormously the incidence of purulent complications.

Arnold Pines

1500. **Bronchial Carcinoma. Effect of Radiotherapy on Survival**

J. R. BIGNALL. *Lancet* [*Lancet*] **1**, 876–879, June 9, 1956. 18 refs.

Stating that "there is no indubitable evidence that radiotherapy prolongs the life of patients with lung cancer" the author points out that a clinical trial in which patients were allocated at random to treated and untreated groups would hardly be justified. However, by a study of the records of the Brompton and the Royal Marsden Hospitals, London, something like such a trial has been simulated, and in this report the survival time of 207 patients treated by radiotherapy is compared with that of 248 who were not so treated, the groups being selected to be as far as possible alike in the factors known to influence survival. They included only patients without evidence of extrathoracic metastases who had lived at least one month after the first examination and in whom the time of appearance of first symptoms was known.

The greatest difference was found in those without mediastinal metastases who were treated by radiotherapy with 4,000 r or more; of these, 35% survived for one year and 15% for 2 years, whereas the corresponding figures in the untreated group were 24% and 6% respectively. In patients with mediastinal metastases the difference was less, while the pattern of survival of those treated with less than 4,000 r was almost identical with that of patients in the untreated group.

After weighing up the possibility of differences arising from selection and random sampling variations, the author concludes that radiotherapy probably caused an increase of less than 10% in the proportion of patients surviving one year after diagnosis, and of less than 5% in those surviving for 2 years, even in the most favourable cases treated with the higher doses. *T. Semple*

1501. **Smoking Patterns and Epidemiology of Lung Cancer in the United States: Are They Compatible?**

W. HAENSZEL and M. B. SHIMKIN. *Journal of the National Cancer Institute* [*J. nat. Cancer Inst.*] **16**, 1417–1441, June, 1956. 3 figs., 26 refs.

The investigation here reported from the U.S. National Cancer Institute, Bethesda, Maryland, was designed to test whether the reported observation of an association between smoking and an increased risk of cancer of the lung in studies on selected groups of patients and healthy individuals was valid for larger populations and compatible with variations in the distribution of lung cancer presumably valid for generalization to larger populations. Data concerning the incidence of lung cancer in different population groups were obtained from several special morbidity studies and from the national mortality statistics for the U.S.A., while the distribution of smoking patterns in the U.S.A. was determined by examination of a sample of 45,000 persons aged 18 years and over, representative of the whole population. The possibility of a relationship between these two sets of data was tested by applying estimates of the relative risk of lung cancer in different categories of smokers and non-smokers, derived from the studies on selected groups mentioned above, to various components of the whole U.S. population and comparing the figures thus "predicted" for the relative mortality in these components with those derived from morbidity and mortality statistics.

In this way the predicted and observed ratios of mortality from lung cancer between the two sexes, urban and rural populations, white and non-white populations, and different regions and cohorts of the population were compared. While correspondence was generally good, the observed sex ratio and the urban : rural ratio for men were appreciably higher than the predicted ratios. The male : female ratio predicted for persons aged 35 years and over was 2·4:1, whereas the ratio observed was of the order of 5:1. Women, however, tend to start smoking at a later age than men, and when allowance was made for the consequent difference in exposure—assuming that the risk of lung cancer is directly proportional to the total amount smoked—the predicted ratio rose to 3·6:1. In the authors' opinion the remaining male excess may result from a basic sex difference in mortality from neoplastic disease in general. The predicted urban : rural ratio for men aged 35 years and over was 1·13:1 against an observed mortality ratio of 1·85:1. A small part of the excess urban mortality might be attributable to overstatement of urban mortality from all causes, but in the authors' opinion the major part represents "a manifestation of multiple environmental factors in lung cancer". *Richard Doll*

Otorhinolaryngology

1502. **Audiometric Measurements by Electroencephalography**

A. J. Derbyshire, A. A. Fraser, M. McDermott, and A. Bridge. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 467–478, Aug., 1956. 6 figs., 19 refs.

At Harper Hospital and the Children's Hospital of Michigan, Detroit, the authors have determined the hearing threshold of 250 patients aged between 3 months and 27 years, most of whom were " non-communicating " pre-school children, by means of the electroencephalogram (EEG). Briefly, the technique consisted in stimulating the sleeping child, in a room shielded from external noise and with a fairly constant ambient noise level, with pure tones for 5-second periods at different intensities and observing any resulting change in the EEG. Sleep was induced with quinalbarbitone (" seconal ").

It was found that the response to a pure tone consisted of four components—an " on " effect (usually a K complex) with 0·1 to 3 seconds latency, a continuous effect, an " off " effect within 2 seconds of cessation of the stimulus, and a delayed reaction (arousal) 5 to 30 seconds later. When any two or more of these components were present the response was considered positive, and any intensity of stimulus which gave a positive response on 50% or more of several presentations was regarded as being above the threshold. Threshold values determined in this way on 22 selected patients whose auditory performance was well known differed from those obtained by a standard audiometric technique by an average of ±18 db. (S.D. 14·7 db.). The type of response obtained varied considerably with age, intensity of stimulus, and depth of sleep. The EEG changes, which were diffuse, could be duplicated with other sensory stimuli, and occurred throughout the age-range tested, appear to be the result of a simple arousal mechanism. The authors consider that audiometric readings obtained in this way may be of clinical value when combined with other information, and the electroencephalographic method may indeed provide the only means of audiometry in infants and handicapped children who cannot communicate. *John N. Walton*

1503. **Epidemiological Approach to the Etiology of Cancer of the Larynx**

E. L. Wynder, I. J. Bross, and E. Day. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1384–1391, April 21, 1956. 7 figs., 24 refs.

This paper from the Sloan–Kettering Institute and Cornell University Medical College, New York, summarizes some of the results so far obtained in studies carried out jointly by workers in the U.S.A., India, and Sweden of the role of environmental factors in the aetiology of cancer of the larynx. The American data were collected from 209 white male patients with laryngeal cancer, from 209 control subjects with other diseases matched for sex, age, colour, " hospital status ", religion, and education, and from 132 white male patients with epidermoid cancer of the lung, and are analysed at some length. The Indian data, covering 132 patients with intrinsic carcinoma of the larynx together with an unspecified number of control subjects, are mentioned briefly, while preliminary data only were available for study from Sweden.

Analysis of the American data showed that the smoking habits of the patients with laryngeal cancer in terms of the quantity of tobacco consumed were similar to those of the patients with cancer of the lung, there being relatively few non-smokers and many heavy smokers in both groups, but were sharply differentiated from those of the control subjects. In this respect there was no difference between patients with intrinsic and those with extrinsic cancer of the larynx. On the other hand there was a higher proportion of cigarette smokers and a lower proportion of cigar and pipe smokers among the patients with intrinsic cancer of the larynx and those with cancer of the lung than among those with extrinsic cancer of the larynx and those in the control group. Heavy consumption of alcohol was commoner among patients with laryngeal cancer than in either of the other two groups, and this was particularly marked in patients with extrinsic cancer. There was no appreciable difference between the proportions of light and moderate drinkers in the three groups, so that, in contrast to tobacco, there would appear to be a threshold (of the order of 7 oz. (200 ml.) of whisky a day) below which alcohol consumption is not associated with the development of cancer of the larynx. No distinct association was found between the incidence of laryngeal cancer and voice strain, occupation, previous disease, or nutrition, but poor dental hygiene was noted more frequently in patients with both types of laryngeal cancer and in those with lung cancer than in the control subjects.

An association between the smoking and chewing of tobacco and extrinsic cancer of the larynx was also demonstrated in the Indian data (cases of intrinsic laryngeal cancer being too few for analysis). The preliminary Swedish data for men with laryngeal cancer showed an association with tobacco similar to that found in the U.S.A., but those for women with extrinsic cancer of the larynx showed no such association, the disease in the majority of cases being apparently related to sideropenic dysphagia. *Richard Doll*

1504. **Results of Mobilization of Fixed Stapedial Foot Plate in Otosclerotic Deafness**

S. Rosen. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 595–599, June 16, 1956. 3 figs., 6 refs.

Urogenital System

1505. **Renal Function after Recovery from Acute Renal Failure**

J. T. FINKENSTAEDT and J. P. MERRILL. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1023–1026, May 31, 1956. 4 figs., 16 refs.

The authors have followed up, for periods of up to 6 years, 16 patients who had recovered from acute renal failure (mostly due to transfusion reaction, poisoning with mercury or carbon tetrachloride, concealed accidental haemorrhage, or shock). One patient subsequently developed periarteritis nodosa and showed progressive renal failure. The others maintained good clinical recovery, urinary concentration and phenolsulphonphthalein excretion returning to normal within 6 months. However, clearances of inulin, *para*-aminohippurate, and urea and maximum tubular clearance of *para*-aminohippurate remained, in most cases, below the lower limit of normal.

K. G. Lowe

1506. **The Prognostic Significance of Globulinuria in the Nephrotic Syndrome. An Electrophoretic Study of Urinary Proteins in the Nephrotic Syndrome and Acute Glomerulonephritis**

W. HEYMANN, C. GILKEY, and M. LEWIS. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 570–576, June, 1956. 7 figs., 19 refs.

The significance of the urinary protein content in the prognosis of the nephrotic syndrome was evaluated in 32 children with nephrosis and 11 with acute glomerulonephritis in an investigation carried out at Western Reserve University School of Medicine, Cleveland, Ohio. The urinary total protein content was determined by the method of Shevky and Stafford on 24-hour specimens of urine kept without preservative in an ice-box during the period of collection, and electrophoresis was performed by the Tiselius method, using barbitone buffer and adjusting the protein concentration to 1·5%, the determinations running for 3 hours at 15 mA and 1·5° C. In 8 of the nephrotic cases urinary protein studies were carried out before and again 3 to 4 days after a reduction in proteinuria induced by cortisone or ACTH (corticotrophin); in the 11 cases of glomerulonephritis, estimations were made within 2 weeks of onset of the disease.

The results showed that the urinary excretion of albumin was not closely related to the outcome of the disease; nevertheless, in the cases of so-called " benign " nephrosis the urinary total protein excretion never exceeded 5·8 g. per day, that of globulin was less than 2 g. per day, and the albumin:globulin (A/G) ratio was 1·1 or more. However, of the 11 children with glomerulonephritis, the A/G ratio was less than unity in 6. The authors suggest that the more favourable prognosis in this condition is due to the lower concentration of protein in the urine and to the shorter duration of proteinuria. They conclude that determination of the amount of globulinuria and of the A/G ratio are of prognostic value in nephrosis, although they emphasize that wide fluctuations of the A/G ratio occur in the course of the disease and point out also that the excretion of globulin is dependent on urinary output.

L. Capper

1507. **The Effect of Corticotrophin (ACTH) on Ammonia Production in the Nephrotic Syndrome**

G. H. HEIDORN. *American Journal of Medical Sciences* [*Amer. J. med. Sci.*] **231**, 644–654, June, 1956. 28 refs.

In this paper from the Montana Deaconess Hospital and the Western Foundation for Clinical Research, Great Falls, Montana, successful results are claimed for ACTH therapy in 8 patients (aged 4 to 28 years) out of a series of 10 with the nephrotic syndrome. In all 8 a steady increase in urinary excretion of ammonia occurred during the first few days of ACTH administration. On withdrawing the hormone a precipitous fall in ammonia excretion commonly occurred. Concentrations of urinary sodium ion and urinary ammonium ion did not appear to bear an inverse relationship one to the other. ACTH-induced diuresis occurred in three patterns: (1) spontaneous diuresis following ACTH withdrawal; (2) spontaneous diuresis of sodium and water beginning on about the 5th or 6th day after starting ACTH treatment; and (3) diuresis delayed until ACTH had restored renal tubular " sensitivity " to mercurial diuretics. The mechanism of the increase in ammonia production remains uncertain, but reasons are given for concluding that ACTH, as well as the adrenocortical hormones, may augment the production of ammonia from the deamination of amino-acids by specific enzymes in the distal tubular cells. This could come about either by direct stimulation of the deaminating mechanism or by making more substrate (for example, glutamine) available to the system.

The author stresses that although enthusiasm for the use of ACTH in the treatment of nephrotic syndrome is maintained in the light of this evidence, ACTH cannot be regarded as a substitute for treatment with an acid-ash, salt-poor diet, adequate fluid intake, adjuvant use of diuretics where indicated, and education of the patient before, during, and after the use of this hormone.

Adrian V. Adams

1508. **Social Factors in the Aetiology of Nephritis in Childhood**

N. S. CLARK. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 153–155, June, 1956. 7 refs.

The author reports the results of an investigation in which 265 cases of nephritis admitted to the Royal Hospital for Sick Children, Aberdeen, between 1934 and 1952, were studied with particular reference to incidence of the disease in relation to the social class and place of residence (that is, town or country) of the patient. In only 119 cases was it possible to assess accurately the occupation of the father.

The distribution of these patients among the Registrar-General's five social classes showed that an unduly high proportion of cases of acute nephritis occurred in Classes IV and V. A comparison of the numbers of patients coming from urban and rural areas showed that the incidence among the former was nearly double that among those living in the country, assuming that the proportion of children in the two populations was approximately the same. Further, the incidence in the two areas showed a correlation with the degree of overcrowding in those areas. It is suggested that this last factor, which provides increased opportunities for the spread of infection, particularly that of the upper respiratory tract, is responsible for the higher incidence of nephritis in children from poorer homes.

[This interesting study is obviously subject to the criticism that there is no proof that admission to hospital for acute nephritis indicates the true incidence of the disease in the region studied.] *C. Bruce Perry*

1509. **The Prognosis of Nephritis in Childhood**
N. S. CLARK. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 156–160, June, 1956. 17 refs.

In this further study of 265 cases of acute nephritis admitted to the Royal Hospital for Sick Children, Aberdeen, between 1934 and 1952 [see Abstract 1508] it was not found possible to divide these cases into two groups according to the classification of Ellis, and it is suggested that all the manifestations of nephritis are different expressions of one disease process. Of the 265 patients, 20 (7·5%) died within one year of the onset. However, 13 of these cases occurred before 1939 and in many of them death was due to infections which could now be controlled by the use of antibiotics.

Of the 245 survivors, 67 could not be traced, but in the remaining 178 cases fairly complete follow-up information was available. Three of the patients had died 6, 8, and 10 years respectively after the onset of chronic nephritis. Of the remainder, 124 (75%) were in normal health one to 13 years after the onset (115 of these were examined in detail and no abnormality was found), 14 (8%) showed evidence of latent nephritis in the shape of albuminuria, haematuria, or hypertension, while 8 patients (4%) were considered to have active nephritis, as judged by the presence of albuminuria and recurrent episodes of oedema, or of albuminuria, cylindruria, and hypertension; in 19 cases (11%) the actual state was uncertain on account of the discovery of a trace of albumin in the urine. In view of these findings the urine of 34 patients (24 considered "healed", 4 classified as "latent" nephritis, and 6 as "uncertain") was subjected to Addis counts, in 22 cases on two or more occasions. This procedure, which is described in an appendix to the paper, involves the estimation of the protein content and number of blood cells and casts in a 12-hour specimen of urine. These counts revealed no further evidence of latent disease in the 24 "healed" cases, but supported the diagnosis of latent nephritis in the 4 "latent" cases, and indicated that of the 6 "doubtful" cases, 4 were normal and 2 were cases of latent nephritis. (The author felt that the time taken to perform the Addis count did not justify its use for routine purposes.) No correlation could be shown between the initial clinical picture in any individual case and the ultimate result. There appeared to be some indication that a higher proportion of the patients found to have active or latent nephritis at follow-up had had marked hypertension in the initial stages, although many with hypertension recovered completely.

C. Bruce Perry

1510. **Changes in the Serum Proteins in Anuric Tubular Nephritis.** (Variations des protides sériques dans les tubulo-néphrites anuriques)
M. DÉROT, P. PIGNARD, and M. LEGRAIN. *Presse médicale* [*Presse méd.*] **64**, 1307–1309, July 14, 1956. 2 figs., 22 refs.

The changes in the serum protein pattern were investigated at the Hôtel-Dieu, Paris, in 14 adult patients with anuric tubular nephritis, 9 being cases of anuria following abortion, 2 following mercurial poisoning, one a case of post-traumatic anuria, one due to transfusion accident, and the last a case of hepato-nephritis of unknown cause. Total serum proteins were determined gravimetrically and the protein fractions by paper electrophoresis on 65 occasions.

During the acute phase, the total serum protein content was characteristically normal or slightly decreased, being between 6·0 and 7·5 g. per 100 ml. Inversion of the albumin:globulin ratio occurred, this being usually between 0·4 and 0·6, but as low as 0·2 in extreme cases. The reduction in the albumin fraction was both relative and absolute, and was of the order of 35% of the total protein instead of 60%. Likewise, the increase in the globulin fraction was also both relative and absolute, and was associated in particular with very significant increases in the α_1-globulin fraction (of the order of 10% instead of 4%), the α_2-globulin fraction (17% instead of 10%), and γ-globulin fraction (25–30% instead of 14%). In contrast, serum β-globulin levels were usually at the higher limit of normal, being moderately increased on only 5 occasions and greatly increased on only one.

In the initial stages, in cases in which anuria had been the result of haemolysis, a transient hyperproteinaemia lasting between 2 and 4 days was observed. It was established that the sole cause of this hyperproteinaemia was the presence of haemoglobin, existing free in solution in the serum. Hyperproteinaemia was also observed in 3 patients who recovered. It occurred at the time when a profuse diuresis followed the period of anuria, but was generally moderate in degree; it was probably partly the consequence of haemoconcentration and partly the result of the serum albumin level returning to normal while the serum globulin content was still abnormally high. The significance of these changes is discussed from the point of view of their physiological origin and their prognostic import. It is speculated that in the future the correction of an abnormal electrophoretic picture may become part of a therapeutic rationale, analogous to the correction of ionic imbalance as used to-day. *Adrian V. Adams*

Endocrinology

THYROID GLAND

1511. **Hypothyroidism Due to a Congenital Anomaly of Hormonogenesis.** (L'hypothyroïdie par anomalie congénitale de l'hormonogénèse)
M. Lelong, R. Joseph, P. Canlorbe, J. C. Job, and B. Plainfossé. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] 13, 341–385, 1956. 20 figs., 24 refs.

Some hypothyroid children show an increased, or at least normal, thyroid fixation of radioactive iodine (^{131}I) —an observation which excludes athyroidism, and suggests a disturbance of hormonogenesis. The authors describe 5 such cases seen at the Hospitals of St. Vincent-de-Paul and Enfants Malades, Paris, since 1950, and review in detail 46 similar cases recorded in the literature.

The first patient was a girl aged 10 in whom a large nodular goitre appeared 6 years after the onset of hypothyroidism, which occurred about the age of 3 years. An increased uptake of ^{131}I by the gland was established. After biopsy examination of the thyroid gland, the making of autoradiographs, and titrations of plasma iodine content and of iodine compounds in the thyroid gland, a hemithyroidectomy was performed 48 hours after ingestion of 1,000 microcuries of ^{131}I. Biopsy examination and autoradiography showed extreme anatomical and functional heterogeneity. The gland consisted of a series of nodules, some dense and white, others cystic. Histologically, it was an adenoma, with some vesicular areas and other areas showing a dense vascular sclerosis. Autoradiographs revealed that the ^{131}I was concentrated in the vesicular zones. Chromatographic studies and chemical analyses showed normal fixation of mineral iodine, good synthesis of mono- and di-iodotyrosine, but an almost complete absence of thyroxine and triiodothyronine. After the hemithyroidectomy and with adequate thyroid medication the remaining part of the goitre quickly disappeared. The other 4 cases were not associated with goitre, and investigations therefore could not be so complete. The essential observation in all 4 was a normal or increased thyroid uptake of ^{131}I.

The authors' conclusions from these 5 cases of congenital anomaly of hormonogenesis, together with the 46 described in the literature, are as follows. (1) The incidence is familial and males and females are equally affected. (2) There is no clear aetiology, such as iodine starvation, goitrogenic medication, or thyroiditis. (3) The symptoms of hypothyroidism appear at a variable age; they are less severe than those of myxoedema resulting from athyroidism. (4) The presence of a goitre is usual only in children over the age of 5 who have received no thyroid medication. (5) The histological character of the goitre is remarkably constant in all cases studied, namely, the larger part consisting of a cellular zone without vesicles or colloid, interspersed here and there with islands of vesicular structure, with abnormal epithelium and scanty colloid. (6) Treatment with thyroid extract acts as it does in athyroidism, having an appreciable effect on somatic development but a variable effect on intellectual development. (7) There is usually normal or increased uptake of ^{131}I. The condition is due essentially to a disturbance of hormone synthesis. Two well defined types are recognized: (1) with defect in the initial stage, that is, in the conversion of mineral to organic iodine; (2) with a defect in the later stage, at which diiodotyrosine is transformed into thyroxine and triiodothyronine.

Kenneth Stone

1512. **Hashimoto's Struma Lymphomatosa. Diagnostic Value and Significance of Serum-flocculation Reactions**
R. W. Luxton and R. T. Cooke. *Lancet* [*Lancet*] 2, 105–109, July 21, 1956. 3 figs., 13 refs.

An investigation of the value of serum flocculation tests of liver function in the diagnosis of Hashimoto's disease is reported. In the authors' view struma lymphomatosa is not uncommon, and a diagnosis of this condition should always be considered when hypothyroidism in a middle-aged woman is accompanied by goitre. Differentiation from carcinoma is essential, since administration of thyroid is the correct treatment for struma lymphomatosa, not subtotal thyroidectomy or *x*-irradiation. The results of the thymol turbidity and colloidal gold tests were abnormal in 21 out of 24 patients; the diagnosis of struma lymphomatosa had been confirmed histologically in 16 of these 24 patients and in the remainder the clinical picture was typical. Partial thyroidectomy had been performed in 6 cases and a course of irradiation had been given in one. The colloidal gold test was more sensitive than the thymol turbidity test, but there was a definite tendency for the results of both to revert to normal with an adequate dosage of thyroid extract. In 5 out of 9 cases the response to the "bromsulphalein" retention test was abnormal, suggesting the presence of liver disease; however, the results of other liver function tests were normal. It is emphasized that the results of liver function tests often remain abnormal after surgery or deep *x*-ray treatment but revert to normal when dried thyroid extract is administered.

It is concluded that the abnormal serum flocculation reactions are due to an alteration in the concentration of γ globulin in the serum, which is a reflection of involvement of the reticulo-endothelial system rather than of the liver. [However, in one of the 4 cases described there was obvious clinical and histological evidence of cirrhosis.] Splenomegaly was observed clinically in 6 patients, in 5 of whom the diagnosis of struma lymphomatosa had been confirmed by the histological findings.

J. N. Harris-Jones

1513. **The Role of Radioiodine in the Treatment of Carcinoma of the Thyroid**

G. HILTON, E. E. POCHIN, R. M. CUNNINGHAM, and K. E. HALNAN. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 297–310, June, 1956. 16 figs., 8 refs.

The authors, working at University College Hospital, London, discuss the selection of cases of carcinoma of the thyroid for treatment with radioactive iodine (^{131}I), the immediate reaction, the sequelae of the treatment, and the results obtained in 73 patients so treated. Details are also given of a further 89 patients who were regarded as possibly having carcinoma of the gland and who were tested with ^{131}I.

In some cases of thyroid tumour, before uptake of ^{131}I can be demonstrated ablation of the gland may be necessary; in the present series 37 out of the 73 patients showed uptake of ^{131}I for the first time only after thyroid ablation. If possible, ablation should be carried out surgically; but this may not be possible or advisable when several previous operations have been carried out or when post-irradiation changes are present in the tissues of the neck, and in such cases ablation can be achieved by treatment with 80 mc. of ^{131}I in one dose. If marked tracheal narrowing is present this dose may be given in equal parts spaced at an interval of 6 weeks. In 9 patients who had received antithyroid treatment no enhanced uptake of ^{131}I was observed. The authors conclude that there is thus no clear evidence that antithyroid drugs given early or late produce a further uptake of ^{131}I once myxoedema has developed.

In the treatment of the cases of tumour, which varied with the individual case, the first therapeutic dose of ^{131}I was given 6 weeks after the ablation dose and consisted of 100 to 150 mc., repeat doses of 150 mc. being given until the proportion of the dose concentrated at the tumour site fell below 0·01% or when uptake of ^{131}I was no longer detectable. As long as the total uptake exceeded 1% then an interval of 6 to 8 weeks between doses was allowed, and when the uptake fell to 0·1% the interval was increased to 3 to 4 months. When myxoedema had developed the patient was given thyroxine continuously, except in the 4 weeks preceding each dose.

In cases of papillary carcinoma the authors advise total thyroidectomy followed by administration of ^{131}I. In the follicular type of tumour total thyroidectomy should be performed and followed by treatment with ^{131}I until no further uptake is detected. If total thyroidectomy is impossible then an ablation dose of ^{131}I should be given. In cases in which the growth is undifferentiated postoperative *x*-ray therapy is recommended.

The authors conclude that ^{131}I should be given an important place in the treatment of carcinoma of the thyroid, being in their view the treatment of choice in some inoperable types of carcinoma, especially those which are predominately follicular and which show an adequate uptake after ablation. Although papillary carcinoma can also be controlled by administration of ^{131}I it is too early yet to say whether this is the treatment of choice when the tumour is still localized; however, if metastases are present treatment with ^{131}I is indicated.

D. G. Adamson

1514. **The Low Toxicity of Carbimazole. A Survey of 1,046 Patients**

C. D. BURRELL, R. FRASER, and D. DONIACH. *British Medical Journal* [*Brit. med. J.*] **1**, 1453–1456, June 23, 1956. Bibliography.

The records of all patients treated with carbimazole (" neo-mercazole ") at 12 centres were analysed at the Postgraduate Medical School of London, to provide information about the incidence and nature of toxic reactions to this drug. Almost all the 1,046 patients reviewed were being treated for thyrotoxicosis. About three-quarters of them received an initial daily dose of 20 to 30 mg., the mean duration of treatment was 9·2 months, and in those treated for more than 2 months the usual daily maintenance dose was under 20 mg.

All toxic reactions occurred within the first 2 months of treatment, and none occurred in the 109 patients receiving under 20 mg. a day initially. Major toxic reactions affected 0·5% and minor reactions 1·5% of the 1,046 patients. The usual major toxic symptoms were fever and a rash, often associated with arthralgia; agranulocytosis developed in only one instance. The common minor toxic effect was a rash.

Although cessation of treatment is usually all that is necessary for recovery, in 6 patients with minor reactions the administration of antihistamines caused disappearance of the reaction, permitting continuation of carbimazole therapy. A previous history of allergic disease was given by 6 of the 21 patients who showed toxicity, and patients sensitized to either methimazole (" mercazole ") or carbimazole were usually sensitive to both. It was, however, possible in these cases to continue antithyroid treatment with perchlorate.

The incidence of toxicity of carbimazole was compared with that of other antithyroid substances by analysing published reports, involving in all about 15,000 patients, from which it emerged that the toxicity of carbimazole was much lower than that of any of the other drugs.

H.-J. B. Galbraith

ADRENAL GLANDS

1515. **Phaeochromocytoma. Catechols in Urine and Tumour Tissue**

H. WEIL-MALHERBE. *Lancet* [*Lancet*] **2**, 282–284, Aug. 11, 1956. 16 refs.

The urinary excretion of 3-hydroxytyramine in a case of phaeochromocytoma was increased as much as, or more than, the excretion of noradrenaline. After surgical removal the tumour was found to contain, in addition to adrenaline and noradrenaline, considerable quantities of 3-hydroxytyramine and 3:4-dihydroxyphenylalanine. A second tumour, discovered at necropsy 16 hours after death, contained similar amounts of adrenaline and noradrenaline but very little hydroxytyramine and DOPA.—[Author's summary.]

1516. **Identification of Hydroxytyramine in a Chromaffin Tumour**

M. MCMILLAN. *Lancet* [*Lancet*] **2**, 284, Aug. 11, 1956. 8 refs.

1517. **Primary Aldosteronism.** (Primair aldosteronisme) F. S. P. VAN BUCHEM, H. DOORENBOS, and H. S. ELINGS. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **100**, 1836–1843, June 30, 1956. 8 figs., 16 refs.

Recently Conn (*J. Lab. clin. Med.*, 1955, **45**, 6; *Abstracts of World Medicine*, 1955, **18**, 143) described a new clinical syndrome, primary aldosteronism, in which urinary aldosterone excretion is abnormally high as a result of hypersecretion by the adrenal cortex, usually associated with the presence of an adenoma or carcinoma. The present authors describe a case in a youth aged 17; the condition was causing no symptoms and the case was investigated only when a high blood pressure was discovered during the course of a routine examination. The parents stated that the patient had suffered from excessive thirst since the age of 2 and more recently had been troubled by frequency of micturition during the night. He also complained of generalized headaches and frequent nose-bleeding, and tended to be irritable and bad-tempered.

In this case, unlike previous cases described, there was no evidence of muscular paralysis or even weakness, although there was a myasthenic reaction to faradic stimulation. There was only doubtful evidence of tetany, and alkalosis was absent. Urinary aldosterone excretion (34 μg. per 24 hours) was much greater than normal (1 to 8 μg.) and was also greater than in comparable cases of adenoma of the adrenal cortex. Treatment by subtotal adrenalectomy, followed by the administration of 25 mg. of cortisone daily—subsequently reduced to 12·5 mg. daily—led to this patient's clinical recovery. Biopsy of the adrenal gland revealed hyperplasia affecting mainly the zona fasciculata of the cortex, but the zona glomerulosa was also involved, suggesting that both zones are concerned in the production of aldosterone. *Adrian V. Adams*

1518. **Control of Aldosterone Excretion by Changes in Volume of Body-fluid**
A. F. MULLER, A. M. RIONDEL, and R. S. MACH. *Lancet* [*Lancet*] **1**, 831–832, June 2, 1956. 1 fig., 7 refs.

The acute retention of body fluid brought about by the administration of posterior pituitary extract (vasopressin) has been shown by Leaf *et al.* (*J. clin. Invest.*, 1953, **32**, 868) to be followed by a marked increase in the urinary excretion of sodium. Moreover these authors found that the loss of electrolyte could be prevented by administering either corticotrophin or a low-sodium diet. The present authors, writing from the University of Geneva, suggest that the increased renal excretion of sodium is caused by a fall in the level of aldosterone secretion as a consequence of retention of body fluid.

They have therefore tested this theory experimentally on a healthy man who was maintained on a constant fluid intake and low-sodium diet. Vasopressin was given intramuscularly, and the urine collected for about one week and analysed daily for its sodium, 17-hydroxycorticoid, and aldosterone content. In this subject there was acute retention of fluid and also an immediate decrease in the urinary excretion of aldosterone; a day or two later the urinary output of sodium increased. On withdrawal of vasopressin the process was reversed, the urinary sodium excretion again being the last to respond; the 17-hydroxycorticoid excretion remained constant throughout. The authors conclude that aldosterone secretion is controlled by the volume of body fluid, although it can also be influenced by corticotrophin independently. *Nancy Gough*

DIABETES MELLITUS

1519. **The Effects of Glucagon on Carbohydrate Metabolism in Patients with Diabetes Mellitus**
A. BOGOCH and H. W. MCINTOSH. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 875–881, June 1, 1956. 7 figs., 8 refs.

The response to glucagon has been studied in 7 insulin-treated diabetics, in varying degrees of control, at the Shaughnessy Hospital, Vancouver, British Columbia. Six of these patients were over 68 years of age and 2 were obese. After a 12-hour fast 2 ml. of glucagon was given intravenously in saline over 30 minutes, the venous blood sugar content being estimated at intervals during the next 2½ hours. Liver function tests and blood pyruvic and lactic acid levels were also determined. Each patient was studied more than once while taking insulin and on the day of its omission. Results, which were reproducible in individual cases, and case histories are detailed. The rise in blood sugar level was greater when the diabetes was well controlled than when insulin was withdrawn, irrespective of the fasting blood sugar level. Plasma pyruvate levels did not change, but there was a slight fall in lactic acid levels as the tests proceeded. There appeared to be no correlation between the blood sugar level and the duration of diabetes, insulin needs, or hepatic function.

It is concluded that the hyperglycaemic response to glucagon depends not only on the degree of diabetic control, but also on the state of nutrition and possibly endogenous insulin production. Glucagon may also help to protect against insulin-induced hypoglycaemia. *Kenneth Gurling*

1520. **Hypoglycaemic and Antidiabetic Sulphonamides**
F. G. YOUNG. *British Medical Journal* [*Brit. med. J.*] **2**, 431–432, Aug. 25, 1956. 20 refs.

The discovery and development of the antidiabetic sulphonamides are described and their mode of action discussed in this paper from the University of Cambridge. These drugs appear to act not by inhibiting the formation of glucagon in the α cells of the islets, as was first suggested, but either as non-competitive inhibitors of hepatic insulinase, so that the destruction of insulin is, at least in part, prevented, or by stimulating its secretion.

The author found that "BZ 55" (carbutamide) given by mouth relieved the diabetic condition permanently in a cat which had been made diabetic by the administration of growth hormone (metahypophysial

diabetes) and had shown no sign of complete remission over a period of many months. He makes the interesting suggestion, relating the antidiabetic to the antimicrobial properties of sulphonamides, that insulin may in part be destroyed by the proteolytic action of bacteria in the liver, so that if these bacteria are killed by the sulphonamide the rate of destruction of insulin will be reduced. *H. E. Holling*

1521. **A Clinical Trial of BZ 55**
L. J. P. DUNCAN, J. D. BAIRD, and D. M. DUNLOP *British Medical Journal* [*Brit. med. J.*] **2**, 433–439, Aug. 25, 1956. 10 figs., 11 refs.

The results are reported from the University of Edinburgh of a trial of " BZ 55 " (carbutamide) in the treatment of mild diabetes mellitus in 5 male and 60 female patients over the age of 45. Cessation of insulin treatment led to the withdrawal of 20 of these patients from the trial—10 because it was found that their diabetes could be controlled by diet alone, 7 because of ketosis, and 3 because of a severe degree of hyperglycaemia—and another was withdrawn because BZ 55 caused a drug fever.

Of the remaining 44 patients, 33 were effectively controlled with BZ 55 in doses of 1 to 1·5 g. daily, continuous rather than intermittent treatment being required. It was shown that the effect of BZ 55 is to reduce the fasting blood glucose level, glucose tolerance being unchanged.

While the new treatment may be useful particularly for the control of middle-aged or elderly, non-obese patients suffering from mild diabetes which cannot be controlled by diet, it is emphasized that patients with ketosis seldom respond to the drug. Minor toxic effects were encountered in several cases, and thrombocytopenia occurred in 8 others, with purpura in 2.
H. E. Holling

1522. **Trial of an Oral Hypoglycaemic Agent in Diabetes**
F. W. WOLFF, G. A. STEWART, M. F. CROWLEY, and A. BLOOM. *British Medical Journal* [*Brit. med. J.*] **2**, 440–445, Aug. 25, 1956.

In a trial of " BZ 55 " (carbutamide) carried out at the Whittington Hospital, London, its effects on 45 diabetics, normally controlled with insulin, were observed, the group containing a preponderance of middle-aged or elderly female patients. Successful treatment was indicated by a fall of the fasting blood glucose content to normal levels and the disappearance of glycosuria, which occurred in 19 cases. The 26 patients in whom BZ 55 treatment was unsuccessful all had a fasting blood sugar level of over 275 mg. per 100 ml. after stopping insulin, their average insulin requirement was greater than that of the successful group, and they had a tendency to develop ketosis. During the test period the average level of sulphonamide in the blood was the same in both groups, each of which received a maintenance dose of 1 g. daily, but the rate of renal excretion of conjugated sulphonamides was less in those cases in which treatment was successful. Skin reactions developed in 5 cases. *H. E. Holling*

1523. **Clinical Trial of the New Oral Hypoglycaemic Agent BZ 55**
J. A. HUNT, W. OAKLEY, and R. D. LAWRENCE. *British Medical Journal* [*Brit. med. J.*] **2**, 445–448, Aug. 25, 1956. 6 refs.

A series of 21 patients with diabetes attending King's College Hospital, London, were selected to cover a wide range of age, weight, and severity and duration of the disease and their response to " BZ 55 " (carbutamide), given in place of, or in addition to, insulin, was tested. The response was classified as " good " in 9 cases, and " moderate " in 6, the maintenance dose being 1 g. daily, and in 6 there was no response even when this dose was increased. The fall in blood sugar level caused by a test dose of 50 mg. of BZ 55 per kg. body weight given to the fasting patient bore some relation to the response to subsequent treatment, but did not provide an entirely reliable guide. Failure to respond to BZ 55 was noted particularly in young diabetics, in those requiring more than small doses of insulin, and those in whom ketosis occurred after the withdrawal of insulin. A good response was more often found in those in whom diabetes had developed after the age of 40, but otherwise the effect of BZ 55 was not related to the duration of the diabetes or of insulin treatment. A further series of 17 patients, selected on the basis of these findings, all responded satisfactorily. *H. E: Holling*

1524. **BZ 55 in Diabetes**
J. M. MCKENZIE, P. B. MARSHALL, J. M. STOWERS, and R. B. HUNTER. *British Medical Journal* [*Brit. med. J.*] **2**, 448–451, Aug. 25, 1956. 4 figs., 3 refs.

A trial of " BZ 55 " (carbutamide) in the treatment of diabetes is reported from the University of St. Andrews in which the effect of the drug was investigated on 20 patients, 16 of whom could not be controlled by diet alone, but did not require large doses of insulin and had never developed ketosis, while 4 required insulin to avoid ketosis, BZ 55 being given in addition.

A satisfactory response to a maintenance dose of 0·5 g. of BZ 55 12-hourly was obtained in 10 of the patients with mild diabetes, while the 4 who received BZ 55 in addition to insulin were better controlled. Studies of differences in arterial and venous blood sugar levels and of changes in serum inorganic phosphorus level provided no evidence that BZ 55 increased the peripheral action of insulin. *H. E. Holling*

1525. **Hypoglycaemic Sulphonamides in Treatment of Diabetes**
G. WALKER, W. L. B. LEESE, and J. D. N. NABARRO. *British Medical Journal* [*Brit. med. J.*] **2**, 451–452, Aug. 25, 1956. 2 figs., 3 refs.

A series of 24 stable, middle-aged diabetics were treated at the Middlesex Hospital, London, with " BZ 55 " (carbutamide) in a maintenance dose of 1 g. daily. The response was satisfactory in 23 cases, but in 2 treatment had to be stopped because a generalized rash developed. The patient who responded poorly subsequently developed a severe neutropenia. One patient developed mild hyperthyroidism. *H. E. Holling*

1526. **The Value of BZ 55 in Control of Diabetes**
I. MURRAY and I. WANG. *British Medical Journal* [*Brit. med. J.*] **2**, 452–454, Aug. 25, 1956. 1 ref.

Successful control of the blood sugar level followed the administration of "BZ 55" (carbutamide) in a maintenance dose of 1 g. daily in 11 of 23 patients with diabetes treated at the Victoria Infirmary, Glasgow. All these patients developed the disease after the age of 45. The drug was ineffective in 2 young patients and in 2 others who were suffering from sepsis.

[The results reported in this paper and the 5 others published with it (see Abstracts 1520–1525) confirm previous reports that it is the older diabetic who has never had ketosis and who needs only small doses of insulin who responds to the hypoglycaemic sulphonamides. Altogether 125 (73%) of 170 such patients did so respond. A sulphonamide rash developed during treatment in about 9% of cases, severe leucopenia was reported in one case, and thrombocytopenia in 8.]

H. E. Holling

1527. **The Effect of "BZ-55" on Biochemically Uncontrolled Diabetes without Insulin Treatment**
B. S. LEIBEL. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 979–982, June 15, 1956. 5 figs.

For a trial of the efficacy of carbutamide ("BZ 55") in diabetes the author, at Sunnybrook Hospital, Toronto, chose a group of 5 diabetics who had refused insulin but whose physical health was good, without ketosis or diabetic complications. It was assumed that each of these patients had an "almost adequate" supply of endogenous insulin, and that some response to carbutamide could be expected. The patients were aged 43 to 55 years, and the duration of the diabetes ranged from 3 to 14 years. On four occasions at intervals of one week the blood sugar level was determined with the patient fasting, 2 hours after breakfast, 4 hours after lunch, and 2 hours after supper. After the second occasion administration of carbutamide (0·5 g. 8-hourly) was begun. Of the 5 patients, 3 responded to the drug, as shown by a reduction in the daily blood sugar level one week after administration started and a further reduction one week later. Of the 2 patients who failed to respond, one had ketonuria occasionally before the trial while the other had never had ketonuria.

Denis Abelson

1528. **Extractable Insulin of the Pancreas and Effectiveness of Oral Hypoglycaemic Sulfonylureas in the Treatment of Diabetes in Man—A Comparison**
G. A. WRENSHALL and C. H. BEST. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 968–972, June 15, 1956. 2 figs., 17 refs.

The relationship between the amount of insulin extractable from the pancreas of diabetics at necropsy and the age at diagnosis or the known duration of the disease is discussed in this paper from the University of Toronto. There was little insulin in the pancreas of patients with onset of diabetes in youth, compared with considerable quantities in the pancreas of diabetics with onset later in life. In the latter group the supply of endogenous insulin appeared to fail gradually over the years, the decline being more marked in males. Appreciable amounts of insulin were present in the pancreas of 60 to 90% of patients with onset of diabetes in maturity—a percentage of the same order as the reported percentage of diabetics responding to carbutamide therapy. A similar parallel was observed between the small amount of insulin extractable from the pancreas of diabetics with onset in youth and the lack of success with carbutamide in this group.

The limitations of these comparisons between observations made during life and at necropsy and on subjects variously treated are emphasized. *Denis Abelson*

1529. ***para*-Aminobenzenesulphonamido*iso*propylthiodiazol in the Treatment of Diabetes Mellitus.** (Le para-aminobenzène-sulfamido-isopropyl-thiodiazol dans le traitement du diabète sucré)
A. LOUBATIÈRES, C. FRUTEAU DE LACLOS, and P. BOUYARD. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 2358–2368, July 6, 1956. 4 figs., 19 refs.

The authors report, from the Faculty of Medicine, Montpellier, the clinical results obtained with the antidiabetic sulphonamide, *p*-aminobenzenesulphonamido-*iso*propylthiodiazol (PASIT), in the treatment of 31 diabetic patients who were given this drug together with a diet containing 150 g. of carbohydrate daily. The dosage of PASIT was 9 g. daily (for a patient weighing 60 kg.) divided into 6 doses per day for 3 days, followed by a rapid diminution to 2 to 3g. daily, which was given for the next 6 weeks; then a maintenance dose of 1 to 1·5 g. daily or on alternate days was given for several months. Side-effects of the drug included lassitude, nausea, anaemia, reticulocytosis, leucopenia, and skin rashes, which in most cases were not serious, although in 2 cases severe skin reactions lead to withdrawal of the sulphonamide.

The results could be divided into three categories as follows: (1) A favourable response of 15 patients to the treatment; most of these had the milder type of diabetes with onset in middle age or maturity. (2) No response was obtained in 12 cases; these patients belonged to the insulin-deficient group, who became acidotic unless insulin was given. (3) In the remaining 4 cases only partial improvement was noted. The authors discuss these findings which, they suggest, support the view that PASIT stimulates the secretion of insulin by acting on the β cells of the pancreas. They point out that this drug is not the ideal antidiabetic sulphonamide and urge that further clinical and laboratory research on these lines is required. *I. McLean Baird*

1530. **Adrenal Adenomata in Elderly Diabetics**
J. J. DALY. *Lancet* [*Lancet*] **2**, 710–711, Oct. 6, 1956. 17 refs.

1531. **The Treatment of Diabetic Acidosis: Comparison of Treatment Regimes with and without Parenteral Potassium**
M. R. BEHRER, D. GOLDRING, and A. F. HARTMANN. *Journal of Pediatrics* [*J. Pediat.*] **49**, 141–164, Aug., 1956. 9 figs., 10 refs.

The Rheumatic Diseases

1532. **The Duration of Chorea**
M. H. Lessof and E. G. L. Bywaters. *British Medical Journal* [*Brit. med. J.*] **1**, 1520–1523, June 30, 1956. 2 figs., 7 refs.

In many diseases the efficacy of treatment can be measured in terms of duration of symptoms, and with this in mind the authors, at the Canadian Red Cross Memorial Hospital, Taplow, have analysed the duration of 206 attacks occurring in 170 consecutive patients suffering from chorea. Five patients who died between one and 15 weeks from the onset were excluded from the analysis.

The mean duration of the attacks was 19 weeks and the range between one and 117 weeks. The authors consider that these and other modes of expressing duration are unsatisfactory in a mixed group of patients who are admitted to hospital at varying intervals after the onset of their illness, and they prefer to use the life-table technique, relating the recovery rate at any stage of the disease to the patients under observation at that particular time. Charts are provided to show the differences resulting from such an interpretation. It was found that from the moment the diagnosis of chorea was proven the recovery rate was generally rapid in those patients who were observed to develop chorea while in hospital. It is suggested that abortive attacks may be quite common and may remain unrecognized, and that these may be partly responsible for the large number of cases of mitral stenosis in adult life in which no history of previous rheumatic fever or chorea is elicited.

John Lorber

1533. **Excretion of Hydroxyproline in Patients with Rheumatic and Non-rheumatic Diseases**
M. Ziff, A. Kibrick, E. Dresner, and H. J. Gribetz. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 579–587, June, 1956. 2 figs., 26 refs.

The amino-acid hydroxyproline constitutes 13% of collagen and 1 to 2% of elastin and is present in no other protein of the body. At New York University College of Medicine the daily urinary excretion of this amino-acid was studied in 64 patients, 48 adults and 16 children. Of the adults, 16 had rheumatoid arthritis, 8 had one of the other collagen diseases, 8 were healthy, and the remaining 16 suffered from a variety of non-rheumatic disorders. The colorimetric method of Wiss was employed and was shown to agree well with other methods, including the reliable isotopic derivative technique. Only the total hydroxyproline excretion was determined, since the average free hydroxyproline in urine did not exceed 3% of the total either in the normal subjects or in the patients.

The daily urinary excretion of hydroxyproline in normal adult individuals averaged 21·8 mg. (range 15 to 33 mg.). The amino-acid was present almost entirely in the bound form, which is relatively stable in acid solution, and for the most part was freely dialysable, suggesting that it is a peptide of low molecular weight. The excretion of total hydroxyproline was not influenced by the oral ingestion of up to 4 g. of l-hydroxyproline or l-proline, but was markedly increased (up to 5-fold) by the ingestion of these amino-acids in the form of 28 g. of gelatin. These results suggest that free hydroxyproline is not synthesized into collagen directly, but that proline is first converted into a peptide, is subsequently oxidized to hydroxyproline, and later incorporated into collagen.

No apparent difference was observed in the urinary excretion levels of total hydroxyproline between healthy adults and the patients with the non-rheumatic diseases; the patients with rheumatoid arthritis and other collagen diseases showed values which were somewhat higher than in the normal subjects, but these were not considered significant on account of the wide degree of scatter of the results. In the children, who were aged 5 to 14 years, the excretion of total hydroxyproline was two to three times that in adults, averaging 64 mg. daily (range 38 to 126 mg.), and was associated with a rise in the percentage of this amino-acid in the total amino-acid excretion. This finding is discussed, but is considered to be unrelated to the activity of any particular disease process.

Harry Coke

1534. **The Pathogenesis of the Collagen Diseases.** (Sur le mode de production des maladies du collagène)
A. Delaunay, S. Bazin, and M. Hénon. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **140**, 233–237, April 24, 1956.

In an attempt to elucidate the nature and pathogenesis of the collagen diseases, experiments were carried out at the Pasteur Institute, Paris, in which an acid solution of collagen ("collagen A" of Nageotte) was treated with solutions of various mucopolysaccharides normally present in mammalian connective tissues, such as chondroitin sulphuric acid and heparin, and of various inorganic salts and bacterial extracts. Chondroitin sulphuric acid and heparin, within certain limits of concentration and *p*H, each combined with collagen to form a fibrillary precipitate which disappeared on adding calcium chloride. Of the 11 inorganic salts tested, calcium chloride was found to be incapable of precipitating collagen in any concentration, and ammonium sulphate had a weak precipitating action in high concentrations only, whereas sodium chloride, bromide, iodide, and sulphate, strontium chloride, bromide, and iodide, sodium salicylate, and acid sodium tartrate all precipitated collagen when added in moderate concentrations, some being also active in low, and others in high concentrations. Bacterial endotoxins and their cleavage products varied in their precipitating activity

and in the stability to heat and resistance to calcium chloride of the precipitates obtained. Thus the endotoxins of *Salmonella typhosa*, *S. enteritidis*, and *Escherichia coli* produced poorly formed, microfibrillary precipitates, whereas the products of *Staphylococcus aureus* gave rise to long fibres.

The effect of various combinations of these substances was also studied. The addition of mixtures of heparin and sodium chloride and of chondroitin sulphuric acid and staphylococcal endotoxin caused no precipitation, whereas a mixture of heparin and *S. typhosa* endotoxin added to the collagen solution resulted in the formation of a microfibrillary precipitate resembling that produced by the endotoxin alone, but with different physical properties.

In the light of these observations it is suggested that the abnormality present in connective tissue in the collagen diseases is a derangement of the collagen–mucopolysaccharide bond brought about by the presence of certain electrolytes in non-physiological concentration or of organic substances, especially of bacterial origin, not normally present. *A. Swan*

1535. **Prednisone and Prednisolone in the Treatment of Systemic Lupus Erythematosus**
E. L. DUBOIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 427–433, June 2, 1956. 6 figs., 10 refs.

The author [who is a recognized authority on systemic lupus erythematosus and its treatment] reports from the University of Southern California, Los Angeles, his experience with the new steroids prednisone and prednisolone in the treatment of 31 patients (of whom 26 were female) with this disease; the diagnosis was confirmed by the L.E.-cell test in 25 cases. Steroid therapy had already been established in 21 cases with cortisone or hydrocortisone, the remaining patients being either untreated or receiving antimalarial drugs. Prednisone was given in 13 cases for periods up to 58 months and prednisolone in 9 cases up to 30 months; in the remaining 9 cases both drugs were given in successive courses. The dosage of prednisone ranged from 10 to 120 mg. per day and of prednisolone from 10 to 160 mg. per day.

As judged by the clinical response, haemoglobin level, and suppression of the L.E.-cell phenomenon, prednisone was found to have up to 10 times the potency of cortisone, the average therapeutic ratio being 5 to 1, while it was about 4 times as active as hydrocortisone. Prednisolone was on the average 5 times as active as cortisone. The average maintenance dose of prednisone was 22 mg. per day. The author advises dietary restrictions and the administration of antacids and anticholinergic drugs for all patients receiving large doses of prednisone in order to prevent the high incidence of peptic ulceration previously noted following the use of this steroid. Sodium retention, though less than with cortisone, has also occurred after large doses of prednisone, and low-salt diets were therefore found necessary. One patient in the series developed a duodenal ulcer while undergoing treatment, and a " Cushingoid appearance " was noted in 13 cases and acne in 5. The most serious side-effect of the steroids, however, was the development of severe diabetes mellitus in 2 patients (one of whom had a family history of the disorder), necessitating withdrawal of the steroid or the institution of insulin therapy.

Patients receiving antimalarial drugs before treatment with prednisone continued with this therapy in conjunction with the steroid therapy. Reviewing this series the author suggests that steroid therapy should be reserved for the more severe cases, since salicylates and antimalarial drugs have proved an adequate form of treatment for earlier and milder cases.

J. N. Harris-Jones

1536. **Studies on Periarteritis Nodosa, with Special Reference to Cardiac and Renal Involvement and Possible Aetiological Factors.** [In English]
H. BÄCKMAN. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 441–462, June 20, 1956. 6 figs., bibliography.

The author reports his observations on 14 cases of periarteritis nodosa studied at Turku University, Finland. The diagnosis was confirmed by biopsy in 2 cases and at necropsy in the remainder. The study was mainly directed to the cardiac and renal changes in the disease, and an attempt is made to correlate these with the clinical findings. Before the cases are described, many of them in detail, the historical and aetiological aspects of the disease are discussed.

The cardiac lesions were found predominantly in the myocardium and pericardium, and in the latter site were associated with retrosternal pain and pericardial friction rub. Angina was not common. Congestive heart failure was the cause of death in most of the fatal cases. Renal lesions were both more frequent and more severe than those found in the heart. Typically, arterial obliteration was seen with accompanying areas of infarction, but aneurysms were occasionally present. Urinary abnormalities were found in 11 instances, and in 6 cases there were renal infarcts. Hypertension was observed in 8 of the patients known to have renal lesions, and was generally associated with long-standing renal changes. The erythrocyte sedimentation rate was usually raised, and eosinophilia was found in 4 patients. Involvement of the liver was also present in 3 cases.

J. N. Harris-Jones

1537. **The L.E. Test in Patients Presenting the Clinical Picture of Rheumatoid Arthritis**
S. W. ROSS and E. K. CLARDY. *Southern Medical Journal* [*Sth. med. J.* (*Bgham, Ala.*)] **49**, 553–558, June, 1956. 5 figs., 18 refs.

The L.E.-cell test was carried out at the University of Arkansas School of Medicine, Little Rock, Arkansas, on the blood of 79 patients with rheumatoid or a rheumatoid-like arthritis, and on 12 patients who were known to have systemic lupus erythematosus. In 18 cases a positive L.E. test result was obtained. Comparison with the clinical and physical findings revealed that in all of the 18 patients showing a positive L.E. reaction more body systems (pulmonary, gastro-intestinal, renal, or

cardiovascular) were involved than in those giving a negative L.E. reaction.

Although reluctant to affirm that a positive L.E. test result is pathognomonic of systemic lupus erythematosus, the authors recommend that in every patient presenting with rheumatoid arthritis the L.E. test should be performed, as a positive test may give warning of multi-systemic disease. They add that the present results offer no clarification of the relationship between systemic lupus erythematosus and rheumatoid arthritis.

E. G. Rees

1538. **Hydrocortisone versus Prednisolone in Rheumatoid Arthritis**

M. FISHER. *Lancet* [*Lancet*] **2**, 18–19, July 7, 1956. 4 refs.

At the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases 25 patients with "disabling progressive rheumatoid arthritis" varying in duration from 3 to 28 years were allocated at random for treatment with either hydrocortisone or prednisolone. The average quantities given daily were approximately 50 mg. and 15 mg. respectively in divided doses [presumably by mouth]. [No mention is made of any other therapy employed concurrently.] Assessment was made in each case before starting treatment and again after 12 and 24 weeks—the functional status (graded according to a defined scale), the number of joints actively affected, hand grip (measured with a rolled-up sphygmomanometer cuff inflated to 15 mm. Hg), haemoglobin level, and erythrocyte sedimentation rate being determined, and radiographs taken of the hands and feet.

No statistically significant difference in the results of treatment was found between the two groups, although those obtained with prednisolone were slightly the more favourable. Moderate degrees of dyspepsia occurred in more than half of each group, with one severe case in the group given prednisolone, and moon-face occurred in 9 cases in each group; hypertension developed during treatment with prednisolone in one case, and pitting oedema in 3 cases, 2 being in the prednisolone group. [No mention is made of electrolyte studies during the trial, and it would appear that the patients were given a normal diet.]

The author concludes from her results that prolonged prednisolone therapy is not justified in this type of case.

J. Warwick Buckler

1539. **Seven-year Observations on the Treatment of Arthritis with Hesperidin–Ascorbic Acid**

P. J. WARTER, H. L. DREZNER, D. A. DONIO, and S. HOROSCHAK. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 592–598, June, 1956. 25 refs.

In this paper from the McKinley Hospital, Trenton, New Jersey, and the Sacred Heart Hospital, Allentown, Pennsylvania, the authors claim that the correction of abnormal capillary fragility is important in the management of rheumatoid arthritis and osteoarthritis. For this purpose they use tablets containing hesperidin and ascorbic acid in equal quantities, the underlying hypothesis being that ascorbic acid is required for the formation and maintenance of capillary intercellular cement, and that its utilization for this function requires the presence of hesperidin.

These tablets were employed "as a therapeutic adjuvant" in the treatment of 42 patients with active rheumatoid arthritis who showed evidence of increased capillary fragility in the form of petechiae appearing spontaneously or on the application of a pressure-cuff to the arm. [It is not stated what other forms of treatment were given.] They received initial doses of 400 to 1,000 mg. daily of hesperidin–ascorbic-acid [presumably 200 to 500 mg. of each] according to the severity of their arthritis. This was later reduced to a maintenance dose of 300 mg. daily. Capillary resistance became normal within 2 months in 35 cases, which are reported to have shown a greater improvement than the remainder in respect of weight gain, reduction in erythrocyte sedimentation rate, reduction in joint swelling, and (possibly) increased resistance to upper respiratory tract infection during an observation period of 7 years; 2 patients in the latter group died of unrelated causes during that time. Similar benefits are claimed to have resulted from the administration of 300 mg. of hesperidin–ascorbic-acid daily to 17 patients with various manifestations of osteoarthritis. Improvement in general health and reduction in joint pain were observed.

[The authors' claims are based on clinical impressions only, without controls, and no clear evidence that this treatment has a direct effect on the joint lesions is presented.]

G. H. Blair

1540. **A Contribution to the Study of Juvenile Rheumatism; Ankylosing Spondylitis in Childhood.** (Contributo allo studio del reumatismo infantile: spondilite reumatoide o anchilosante nell'infanzia)

M. LUCCHESI and O. LUCCHESI. *Reumatismo* [*Reumatismo*] **8**, 130–136, May–June, 1956. 7 figs., 5 refs.

Spondylitis ankylopoietica is commonly thought to be a disease beginning at puberty or during adolescence. The authors present 4 cases occurring in children, 2 of which were typical cases involving the whole spine in children aged 11 and 12 years respectively, with a history of stiffness and pain for several years; the third was an early case in a child aged 11. The fourth case, however, occurred in a child aged only 34 months, and was manifested by rigidity and calcification in the cervical spine, associated with generalized Still's disease of 2 months' duration.

The authors consider that rheumatoid arthritis and ankylosing spondylitis are two quite distinct diseases. They suggest that an infantile form of spondylitis ankylopoietica occurs more frequently than is thought, but is usually confused with rheumatic fever, the spinal changes becoming apparent only during adolescence. The differential diagnosis is discussed.

David Friedberg

1541. **Radiological Appearances in Ankylosing Spondylitis.** (Les aspects radiologiques de la spondylarthrite ankylosante)

P. LOUYOT. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 2290–2300, July 2, 1956. 16 figs.

Physical Medicine

1542. **Afferent Influences in the Management of Spastic Paresis**
R. C. PSAKI and W. J. TREANOR. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **37**, 214–217, April, 1956. 8 refs.

The authors outline a programme of rehabilitation in cases of spastic paresis which aims at the control of afferent impulses from the paretic muscles and is claimed to be an improvement on the methods that are usually employed.

This programme has been used in the management of 125 cases of spastic hemiparesis. Standing was encouraged until the extensor muscles were able to support the body weight. Then walking was curtailed until the patient was able to perform 90-degree knee flexion in the standing position without concomitant hip flexion, another reason for this restriction being that standing was found " to facilitate hypertonus in the arm, and to be detrimental to the reeducation of the recalcitrant extensor muscles ". All efforts were directed to reeducation of the flexors of the leg and the extensors of the arm; the antagonists were totally ignored. Occupational therapy involving the use of the hand was found to encourage flexor rather than extensor movements of the arm in the early stages of recovery, so that only therapy involving gross movements of the arm was employed.

Injections of 1% " xylocaine " (lignocaine) to block hyperactive muscles were found useful in assessing the potential for recovery in the paretic muscles and as a guide to the possible benefit to be gained from surgical interruption of the nerves to the hyperactive muscles (" selective proprioceptive de-afferentation ").

G. S. Crockett

1543. **Physiological Approach to Ambulation in Paraplegia**
E. E. GORDON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 686–688, June 23, 1956. 2 figs., 4 refs.

The intensity of effort involved in walking with crutches was measured at Columbia University in 11 patients with three types of paraplegia. To determine the total energy requirements, oxygen uptake per minute during activity and subsequent oxygen debt, together with blood lactate level, were estimated. The results, which are given in diagrammatic form, indicate that if the neurological lesion is severe, then ambulation can be achieved only with the maximum of effort and at a high metabolic cost to the patient.

The author suggests that patients with a lesion of the cord below the 12th thoracic vertebra or involving only the trunk flexors should be able to walk as a means of progression, but that the more severely disabled should be content with standing or walking only short distances, and so should be trained to lead a life in a wheel-chair. Consequently patients should be selected for ambulation on an anatomical basis. In the case of the more severely disabled emphasis should be shifted from heroic efforts to teach ambulation towards more constructive vocational training.

J. B. Millard

1544. **The Problem of the Long-term Respirator Patient**
H. N. NEU and H. A. LADWIG. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **37**, 351–357, June, 1956. 3 figs., 13 refs.

During the course of 2 years 50 patients with chronic respiratory paralysis due to poliomyelitis were admitted to the Creighton Memorial St. Joseph's Hospital, Omaha, Nebraska. The patients were admitted from 14 days to 8 years after the initial attack of acute infection, and a respiratory aid was needed in every case at the time of admission. In many cases tank respirators could be discarded immediately and cuirass respirators used instead. Rocking beds and intermittent positive-pressure breathing devices were considered of value in maintaining adequate function of the respiratory tract. Most useful among the latter was a simple vacuum-cleaner apparatus, the patient inspiring air through a long plastic tube. Patients were instructed to cough at the end of inspiration to facilitate clearance of the bronchi. Sometimes this procedure caused dizziness, and one patient showed evidence of transitory mediastinal emphysema.

Application of the plastic dome facilitated the use of physical therapy procedures such as breathing exercises and manual stretching of the thorax, trunk, and shoulders. In a few cases loss of pulmonary compliance was prevented by massage and stretching of the intercostal muscles, chest compression, and " rib springing ". An accelerated increase in vital capacity was recorded in several cases when moist heat was applied in a thermostatically controlled cabinet. Exercises with the shoulder wheel appeared to increase the strength of the muscles of the shoulder girdle. As a preliminary to eliminating respiratory aids patients were taught glossopharyngeal breathing. Only minimal side-effects were experienced when the quantity of air forced into the lungs amounted to 2 litres. Psychiatric advice was helpful in the management of psychogenic hyperpnoea.

Following the use of the techniques described 12 patients were enabled to discard their respirators completely.

A. Garland

1545. **The Role of Rehabilitation in a Program for Handicapped Children**
H. M. WALLACE, J. S. TOBIS, R. S. SIFFERT, M. A. LOSTY, and C. H. ELLEDGE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 26–30, Sept. 1, 1956.

Neurology and Neurosurgery

1546. **Relaxant Effects of Meprobamate in Disabilities Resulting from Musculoskeletal and Central Nervous System Disorders: Clinical Observation of Fifty-five Cases**

H. E. GILLETTE. *International Record of Medicine* [*Int. Rec. Med.*] **169**, 453–468, July, 1956. 26 refs.

At the Physical Medicine and Rehabilitation Clinic, Atlanta, Georgia, meprobamate was used as an adjuvant to physiotherapy in 55 patients suffering from various spastic disorders. To assess the efficacy of the drug the patients were divided into two groups: Group 1, 27 patients with musculo-skeletal disorders, among whom were 13 with cervical myositis or fibrositis, 4 with herniated disk, and 7 with "whiplash" injury to the spine (this last injury follows motor-car accidents in which there was an impact from the rear—a common and well-recognized cause of disability in the U.S.); Group 2, 28 patients with disease of the central nervous system, including 16 children and adolescents suffering from cerebral palsy (12 athetoid and 4 spastic) and 7 elderly patients with hemiplegia following a cerebrovascular lesion. At first the drug was given in the recommended dosage for an adult of 800 mg. 3 times a day, but this caused drowsiness, and the dosage was reduced with benefit to 400 mg. 3 times a day. The results were excellent in 11 of the patients in Group 1 and some improvement was noted in all except 2. Of the 28 patients in Group 2, 21 appeared to derive benefit from the drug, there being a reduction in emotional tension in both athetoid and spastic cases of cerebral palsy. The results were not so good in patients with hemiplegia and there was no response in 2 cases of progressive dystonia musculorum deformans. Improvement was generally noted within 3 days of the start of treatment. Drowsiness was the chief side-effect, but in 2 patients an erythema developed during treatment, which, however, subsided as soon as the drug was discontinued.

William Hughes

1547. **The Electromyogram in the Diagnosis of Infectious Neuronitis. With Particular Reference to the Differential Diagnosis between This Disease and Local Neurosurgical Lesions**

A. A. MARINACCI and C. W. RAND. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **21**, 37–48, March, 1956 [received June, 1956]. 6 figs., 1 ref.

The authors have examined "a considerable number" of patients affected with infectious neuronitis, and here present, from the University of Southern California Medical School, Los Angeles, 8 illustrative cases, together with an account of the diagnostic use of the electromyogram in this disease.

The basis of the diagnostic procedure is that denervation can be detected electromyographically in areas far beyond those in which its signs, such as muscle wasting and paralysis, can be recognized clinically. They state that widespread denervation not of segmental distribution, together with the finding of a raised protein level but normal cell count in the cerebrospinal fluid, is very suggestive of infectious neuronitis. In atypical cases the disorder may present clinically as weakness or paralysis of a group of axial trunk muscles, unilateral involvement of a single extremity, or paralysis and weakness restricted to both lower limbs, and these forms may thus simulate such conditions as unilateral intracranial lesions, tumour of the cord, or herniated intervertebral disk. Electromyography is undertaken in such cases over a wide area of the body to determine the specific distribution of denervation, which may vary from very mild to severe. In neuronitis the denervation is widespread, whereas in conditions such as spinal-cord tumour or herniated disk denervation is found only below the level of the lesion. Conditions such as anterior poliomyelitis, transverse myelitis, and motor neurone disease produce denervation with a plurisegmental distribution. Lesions of a plexus or of a peripheral nerve give rise to denervation only in muscles supplied from that source. The authors emphasize that electromyography is a laboratory procedure and that its findings must always be viewed in the light of the clinical picture; it cannot replace a thorough neurological examination and other appropriate procedures.

Kenneth Tyler

1548. **Intraspinal Epidermoid Tumours (Cholesteatomas) in Patients Treated for Tuberculous Meningitis**

C. CHOREMIS, D. ECONOMOS, C. PAPADATOS, and A. GARGOULAS. *Lancet* [*Lancet*] **2**, 437–439, Sept. 1, 1956. 1 fig., 6 refs.

The authors, working at the University Paediatric Clinic, Athens, have seen within the course of 10 months 6 cases of intraspinal epidermoid tumour (cholesteatoma) in children aged between 7 and 12 years who had been successfully treated for tuberculous meningitis 3 to 6 years previously. In all these patients the main symptom was severe pain in the lower back and thighs, which was aggravated by sneezing, coughing, or bending. Neurological signs were inconstant, but included exaggeration of the tendon reflexes on one side or the other; there were no sensory changes. The cerebrospinal fluid (C.S.F.) in one case showed a protein content of 1·5 g. per 100 ml. in the lumbar theca, but the cisternal fluid was normal. In the remaining cases the C.S.F. was either normal or showed only minor abnormalities. Contrast myelography revealed an obstruction in the lower spinal canal in all cases, and at operation in each instance one or more tumours were removed. These were generally white and pearly in appearance and creamy in consistence, and contained numerous cholesterol crystals, keratinized material, and

desquamated and degenerated epithelial cells. In every case the histological diagnosis was cholesteatoma.

Cholesteatomata within the spinal canal are exceedingly rare in children, and the authors therefore argue that in the present cases they must have had some aetiological relationship to tuberculous meningitis or its treatment. As such tumours can be experimentally produced by implantation of epithelial cells by trauma, it is considered likely that in the treatment of the tuberculous meningitis, during which multiple spinal injections were given, epithelial cells were implanted in the spinal canal and that these grew very slowly to produce the tumours. (The authors used lumbar-puncture needles without a stylet.) It is suggested that myelography should be performed on all patients who have had tuberculous meningitis and who later complain of persistent backache.

[A most interesting and original series of observations.] *John Lorber*

1549. **A Study of Gamma Globulins in Dystrophia Myotonica**

H. H. ZINNEMAN and J. ROTSTEIN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 907–916, June, 1956. 5 figs., 18 refs.

Electrophoretic analysis, carried out at the University of Minnesota, Minneapolis, of the serum protein pattern in 12 patients with dystrophia myotonica showed that the value for the γ-globulin fraction was relatively low (5·9 to 16·9%) while that for the β-globulin fraction was relatively high (12·9 to 18·2%). Immunization with polysaccharides of *Diplococcus pneumoniae* Types I and II and typhoid–paratyphoid vaccine raised the serum γ-globulin level of 3 patients from between 5·9 and 6·5% to between 10·6 and 16·1%, thus suggesting that the low γ-globulin values were not associated with a defect in globulin production. Studies of the rate of disappearance of ^{131}I-labelled normal human albumin and γ globulin, performed on 6 patients, showed that γ globulin disappeared more rapidly than in normal subjects, while albumin disappeared at about the same rate. It is suggested, therefore, that the low serum γ-globulin levels in patients with dystrophia myotonica are the result of abnormal metabolism of this protein. *J. E. Page*

1550. **Myasthenia Gravis. A Personal Study of 60 Cases**

H. GARLAND and A. N. G. CLARK. *British Medical Journal* [*Brit. med. J.*] **1**, 1259–1262, June 2, 1956. 18 refs.

A total of 60 patients suffering from myasthenia gravis were seen by the senior author at the General Infirmary at Leeds or in private practice between 1934 and 1955, 7 of whom could not be traced in 1955 for the purposes of this long-term study of the disease. Of the remaining 53, 9 died from myasthenia gravis, the shortest period of survival being one year. Of the 44 survivors, 24 have minimal or no disability, 13 have slight disability, and 7 are moderately disabled. Twelve patients have had purely ocular symptoms, while in only 5 cases was there no history of ocular disturbance. Apart from the daily fluctuations and partial remissions characteristic of the disease, complete remissions for periods varying from days to 7 years have occurred in 24 cases, whereas another 24 patients have at no time had a complete remission; in 5 cases a complete history was not available.

The authors consider that "it is quite impossible to forecast the future for any patient, at any stage, with any degree of accuracy". *J. W. Aldren Turner*

1551. **Chronic Postherpetic Neuralgia**

L. S. VAN BLARICOM and G. HORRAX. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 511–515, June 9, 1956. 1 fig., 14 refs.

Because its treatment remains unsatisfactory chronic postherpetic neuralgia receives scant attention in the medical literature. In this paper the authors' therapeutic experience in 35 cases during the past 20 years at the Lahey Clinic, Boston, is described. All the patients were over 40 and the sexes were equally represented. The most frequent sites of the herpes were the thoracic and trigeminal nerves. Most of the patients received a variety of forms of treatment, which included the administration of thiamine, nicotinic acid, belladonna, and phenobarbitone, intradermal injection of procaine or saline, neurectomy, procaine and alcohol block, skin excision, skin undercutting, radiotherapy, rhizotomy, chordotomy, lobotomy, spinal analgesia, intrathecal injection of alcohol, and paravertebral sympathetic block. In spite of this the results were poor. Only one patient obtained complete relief (after posterior rhizotomy), while improvement of some degree was maintained for periods of one year or more in 16 cases and for lesser periods in 20; there was little or no improvement in 16 cases. It is suggested [and probably correctly] that the development of neuralgia may be prevented by vigorous treatment of the herpes in its acute phase with antibiotics to reduce the risk of secondary infection. [As usual, it is suggested that posterior pituitary extract has a satisfactory effect in the acute stage of herpes, though whether this is true is extremely doubtful.] *Hugh Garland*

BRAIN AND MENINGES

1552. **Prognostic Studies in Children with Cerebral Palsy**

E. DENHOFF, R. H. HOLDEN, and M. L. SILVER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 781–784, June 30, 1956. 4 figs., 4 refs.

In a study carried out at the Miriam Hospital, Providence, Rhode Island, the authors have attempted to evaluate the validity of pneumoencephalographic and psychological examinations in predicting the future adjustment of 50 children with cerebral palsy, of whom 35 were spastics, 7 had athetosis, 6 ataxia, and 2 rigidity; the mean age at first examination was 3·2 years (range 4 months to 12 years). Pneumoencephalography carried out by standard methods proved to be a safe procedure, providing meticulous attention was given to the patient's fluid needs before and after the examination. Seven

types of pneumoencephalogram were recognized, these showing respectively bilateral cerebral atrophy (7 cases), bilateral cortical atrophy (8), unilateral cerebral atrophy (9), unilateral cortical atrophy (3), bilateral cerebral and cortical atrophy (6), cerebellar atrophy (8), and no apparent brain damage (9 cases). The predictions as to future adjustment were based on the extent and location of the damage demonstrated, and 2 years later they were compared with each child's progress as assessed independently by a paediatrician.

The revised Stanford–Binet test (for mental age 1½ years) was given to all children who were able to respond, while the Vineland social-maturity scale was used for the infants. The prognosis was considered to be good if the intelligence test showed an I.Q. above 85%, fair if it was between 60 and 85%, and poor if below 60%.

The authors comment that predictions are easy to make and proved reliable for children of average intelligence and mild handicap and also for the mentally deficient and severely handicapped. They were less reliable for children of intermediate status, and in these cases the authors believe that the pneumoencephalogram can often help to clarify the prognosis. It is their experience that the attitude of the patient's family contributes materially to the child's progress; thus a good environment can counteract to some extent the handicaps of a poor physical state, whereas an unfavourable one may interfere with the achievement of maximum function.

[This is a disappointing paper. What the authors say about intelligence testing is well known and recognized. But they omit entirely to discuss the difficulty of assessing intelligence accurately in, for instance, an athetoid patient who has unintelligible speech and no motor control.] *N. S. Alcock*

1553. **Etiologic Factors in Adult Convulsions. An Analysis of 689 Patients Whose Attacks Began after Twenty Years of Age**

S. LIVINGSTON. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1211–1216, June 28, 1956. 31 refs.

The presumed aetiological factors in 689 patients who first experienced a major convulsive (grand-mal) attack after the age of 20 years are discussed in this paper from the Johns Hopkins University and Hospital, Baltimore. The patients were examined for the presence of neurological or metabolic diseases before they were admitted to an epileptic clinic, where 152 were followed up for at least 5 years and 490 for 10 years or longer. The convulsions were generalized in 534 patients, generalized with a focal onset in 84, and completely focal in 71. None of the patients, 581 of whom were males, had had any type of seizure previously. In 162 the epilepsy was symptomatic due to cysticercosis (1), brain tumour (2), brain abscess (2), birth trauma (4), trauma after birth (17), pregnancy (8), neurosyphilis (11), alcohol (28), psychogenic factors (6), or hypertension and arteriosclerosis (83). The remaining 527 patients were considered to have cryptogenic (idiopathic) epilepsy.

The author emphasizes that " cryptogenic epilepsy and other presumptive causes for convulsions " should be considered only when exhaustive efforts have been made to rule out every possible aetiological factor. The indications for pneumoencephalography and angiography are discussed. *J. B. Stanton*

1554. **Infected Subdural Effusions**

J. HANKINSON and L. V. AMADOR. *British Medical Journal* [*Brit. med. J.*] **2**, 122–126, July 21, 1956. 4 figs., 12 refs.

The authors briefly review the literature on infected subdural effusions and present short reports of 5 cases seen at the Children's Memorial Hospital, Chicago, 4 of which occurred in children under one year of age as a complication of meningitis. In 2 cases the infecting organism was *Haemophilus influenzae*, in one a meningococcus, and in the other no organism was recovered. The fifth case occurred in a boy aged 4½ who had undergone operation for bilateral subdural haematomata at the age of 6 months. The old haematoma cavities had become infected 4 years later following a respiratory infection; although there was abundant pus, no organisms were recovered in this case either.

The authors consider that subdural effusions complicating meningitis are not uncommon and that if untreated may delay or prevent recovery and even lead to subsequent retardation of development as a result of damage to the brain. Persistent fever, repeated convulsions, gross neurological deficit, tenseness of the fontanelles, and separation of the cranial sutures are all considered good indications for subdural exploration. This should be repeated over several days, and if the amount of pus is not decreasing or there is evidence of a definite subdural membrane, then craniotomy should be undertaken to provide adequate drainage and remove the membrane. The authors also stress the fact that some of these effusions are situated posteriorly and may be missed on routine subdural tapping through the anterior fontanelle. If there is any doubt, posterior parietal burr-holes should be made on either side. *Brodie Hughes*

1555. **Subacute Progressive Encephalitis; Clinical and Electroencephalographic Observations in 23 Cases.** (Encéphalite subaiguë progressive; constatations cliniques et électroencéphalographiques dans 23 cas)

A. M. HAMOEN, H. HERNGREEN, W. STORM VAN LEEUWEN, and O. MAGNUS. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **94**, 109–119, Feb., 1956 [received July, 1956]. 9 figs., 12 refs.

Of the 23 cases of subacute progressive encephalitis here described from three Dutch neurological clinics, 17 occurred in boys and 6 in girls, the age of onset ranging from 3 to 18 years. All the patients suffered from muscular spasms and changes in tonus, in some cases amounting to ballismus, and 15 have so far died after illnesses lasting from 3 to 27 months (mean 13 months). In all cases the changes in the cerebrospinal fluid were regarded as characteristic, namely, a paretic type of response to the Lange test, an increased protein content, and sometimes an increase in the number of cells. The changes in the electroencephalogram were similar to those reported by other authors. Thus, at first the alpha rhythm was preserved, but later gradually

disappeared. In 9 cases asymmetry of the alpha rhythm was thought to be related to asymmetrical progress of the disease. A clear theta rhythm was present in 9 cases and in 2 it was asymmetrical, while bilateral delta activity was seen in 8 cases and was asymmetrical in 2. Focal changes were present in 11 cases.

The typical paroxysms were seen in all the patients, but in 2 they occurred only during hyperventilation; in one of these cases photic stimulation at 8 to 10 c.p.s. also induced an attack. The interval between the paroxysms ranged from 4 to 30 seconds, in some cases being remarkably regular. The most constant element of the paroxysm was activity at 1 to 3 c.p.s. and up to 1,400 microvolts in amplitude, preceded in 15 cases by a positive deflection. The paroxysms were usually bisynchronous and asymmetrical. They were diffuse in 15 cases, frontal in 5, and occipital in 2, and diminished, but did not always disappear, during sleep. Post-mortem histological examination of the brain in 7 cases showed the presence of demyelination, gliosis, and a mesenchymatous reaction affecting the cortex and white matter. In one case necrotic foci up to 3 cm. in diameter were present. Characteristic inclusions were seen in 3 cases and atypical inclusions in one.

The authors believe that in these patients there is no relation between the paroxysms and sleep spindles. They agree with Hess that there are periodic changes in the excitability of the cortex, the subcortical structures, and the cord, but they found no histological evidence to suggest that the reticular system is responsible. They are of the opinion that a process of disinhibition may underlie the paroxysmal features of the disease. *L. G. Kiloh*

1556. **Early Diagnosis of Cerebral Meningiomata**
G. F. Rowbotham. *Newcastle Medical Journal* [*Newc. med. J.*] **25**, 18–21, June, 1956.

Among 700 consecutive cases of cerebral neoplasm seen at the General Hospital, Newcastle upon Tyne, there were 61 cases of meningioma. The mean interval between the appearance of the first symptom and admission to hospital was 2·1 years. The first symptoms were headache (29 cases), abnormal neurological signs, focal or generalized epilepsy, and mental changes. Plain radiographs of the skull revealed evidence of a meningioma in 21 instances, including an increase in diploic markings, hyperstasis, erosion, and areas of calcification. In each of the 36 cases in which lumbar puncture was performed there was an increase in the protein content of the cerebrospinal fluid above 80 mg. per 100 ml. In the author's view air encephalography is most helpful in the diagnosis of these neoplasms, but the value of cerebral angiography has not yet been established and the use of radioactive isotopes is still in the experimental stage. He reserves ventriculography for precise location of tumours that have been diagnosed by other means.

In only 40 of the 61 cases was complete removal of the tumour possible, and in 10 of these there was residual disability. The growth was incompletely removed in 16 cases, while in 5 operation was not undertaken because of the patient's serious condition. There were 7 post-operative deaths. The author pleads for earlier diagnosis, either by careful observation for symptoms or signs before the complete syndrome develops, with irreversible cerebral damage, or by the wise use of those mechanical methods of investigation which are painless and without danger. *I. Ansell*

1557. **Surgical Occlusion of Anterior Choroidal Arteries in Parkinsonism. Clinical and Neuropathologic Findings**
R. W. Rand, W. J. Brown, and W. E. Stern. *Neurology* [*Neurology*] **6**, 390–401, June, 1956. 9 figs., 20 refs.

From the Veterans Administration Center (University of California), Los Angeles, 5 cases are described in which Parkinsonism of varied aetiology was treated surgically by clipping and coagulating the anterior choroidal arteries. In 2 patients with unilateral manifestations of the disease the contralateral artery was occluded, while in the remaining 3 patients, who had bilateral signs, the artery on the right was occluded in 2 cases and both arteries in the third. The result obtained was immediate and complete, although temporary, cessation of tremor in 3 out of 4 of the cases and the abolition of rigidity in 2; a transient homonymous quadrantanopsia occurred in one patient and a permanent hemianopsia in another.

The authors discuss the theories of origin of the tremor and rigidity in Parkinsonism and the rationale of treatment by occlusion of the anterior choroidal arteries. They suggest that the rather disappointing long-term results are due to the difficulty of securing a constant degree of infarction in the right place in all cases. The neuropathological findings at necropsy on 2 patients who died 6 weeks and 10 months respectively after operation are described. *J. B. Stanton*

1558. **"Akineton", a New Preparation for the Treatment of Parkinsonism, with Observations on the Objective Assessment of its Effect.** (Akineton, ein neues Mittel zur Behandlung des Parkinson-Syndroms, zugleich ein Beitrag zur objektiven Wirkungskontrolle)
H. Keller. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **132**, 13–23, June, 1956. 3 figs., 4 refs.

The author reports favourable results from the use of "akineton", a drug which is one of the trihexyphenidyl series, in the treatment of 46 cases of various types of Parkinsonism at the University Neurological Clinic, Munich. Its effect on the several manifestations of the disease, namely, rigidity, loss of power, and tremor, was tested objectively. The usual dosage was 1 mg. (half a tablet) three times a day increasing to 6 mg. (3 tablets) three times a day. Side-effects were not serious, the most marked being a notable fall in blood pressure following intravenous administration of the drug during investigation of its effect on tremor. Improvement occurred in most cases, especially in regard to tremor, and some previously disabled patients were able to become independent again in matters such as dressing and getting in and out of bed, while others could walk again unaided. *G. S. Crockett*

Psychiatry

1559. **Life Situations, Behaviour, Attitudes, Emotions and Renal Excretion of Fluid and Electrolytes. II. Retention of Water and Sodium; Diuresis of Water**
W. W. SCHOTTSTAEDT, W. J. GRACE, and H. G. WOLFF. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **1**, 147–159, June, 1956. 10 refs.

This paper reports, from the New York Hospital (Cornell University), New York, a study of the relationship between various emotional states and the renal excretion rates of water and sodium in 5 healthy subjects. The authors summarize their results as follows. " In 94 situations which these 5 subjects perceived as threatening, but which they felt they could meet adequately by alert behaviour and readiness for action, there was a significant decrease in rates of excretion of water and sodium as compared with 119 situations which these same subjects considered neutral and tranquil. In 30 situations which these subjects felt had elicited sudden feelings of release from tension, or sudden relaxation following sustained effort, there was a significant increase in rate of excretion of water but not of sodium as compared with 119 situations which these subjects considered neutral and tranquil." *Desmond O'Neill*

1560. **The Incidence and Prognosis of Endogenous Depression**
C. A. H. WATTS. *British Medical Journal* [*Brit. med. J.*] **1**, 1392–1397, June 16, 1956. 2 figs., 10 refs.

Over a period of 10 years 569 depressive episodes in 529 patients were observed in a semi-rural general practice of some 8,000 patients, 387 (68%) of the episodes being endogenous; of these, 59% were regarded as mild, 24% as moderate, and 17% as severe. The whole series contained 6 cases of suicide and 8 cases of attempted suicide. A year-by-year analysis showed that depressive disorders amounted to 36% of all new psychiatric cases seen, the morbidity being at least 5 new cases per 1,000 population at risk per annum. Only in 27% of the 387 endogenous depressive episodes was the patient referred to a psychiatrist. There was a predominance of women in the whole series, with a male:female ratio of 2:3, but in the age groups over 60 males predominated. The peak incidence for both sexes was in the 45–50 age group.

A follow-up study of the cases of endogenous depression showed that 77% made a good recovery, 9% remained unchanged or were only slightly improved, while 14% deteriorated into a state of chronic hypochondriacal depression, committed suicide, or died in depression. While no sex difference in the prognosis of mild and moderate forms was observed, males with severe depression fared worse than the corresponding female group. Age was important, the outlook for patients under 60 being significantly better than for older patients.

[In many ways general practice provides an ideal laboratory for the observation and study of depressive illness, and this paper makes a valuable contribution to the scanty epidemiological data available on these disorders as they occur in the population at large.]
J. A. Harrington

1561. **An Objective Test which Differentiates between Neurotic and Psychotic Depression**
C. SHAGASS, J. NAIMAN, and J. MIHALIK. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 461–471, May, 1956. 3 figs., 19 refs.

The aim of the investigation here reported from the Allan Memorial Institute of Psychiatry and McGill University, Montreal, was to apply an objective test, the determination of the sedation threshold, to the study of depressive conditions, with particular reference to their separation into neurotic and psychotic forms. The sedation threshold (Shagass, *Electroenceph. clin. Neurophysiol.*, 1954, **6**, 221; *Abstracts of World Medicine*, 1954, **16**, 500) is defined as the amount of amylobarbitone, in mg. per kg. body weight, injected under defined conditions, that is needed to produce an increase in frontal electroencephalographic activity coinciding with the onset of slurred speech. Altogether 182 patients were examined, 76 being diagnosed as psychotic depressives (10 of whom had recently received electric convulsion therapy (E.C.T.)), 7 as depressed schizo-affectives, 10 as " hysterical " depressives, 47 as neurotic depressives, and 42 as suffering from anxiety states; most of the patients in the last two groups showed obsessional personality characteristics.

The authors had previously shown that the sedation threshold is correlated positively with manifest anxiety and negatively with impairment of ego functioning. In the present series the threshold in most cases of neurotic depression and anxiety state was high (4 mg. per kg. or more), being low (3·5 mg. per kg. or less) in most other cases, this difference demonstrating that " neurotic and psychotic depressions represent two independent populations with respect to sedation threshold ". It was found that the threshold tended to increase after E.C.T., that it was unrelated to the presence of agitation or retardation in psychotic cases, and that it did not enable anxiety states to be distinguished from neurotic depression (contrary to an earlier finding). The threshold was unrelated to the number of previous depressive episodes or to age. The short-term clinical effects of E.C.T. were determined in 96 cases, the results showing that patients with a low threshold (psychotics) were more likely to experience a full remission of symptoms.

The authors claim that these findings support the validity of the separation of depression into distinct neurotic and psychotic types, and suggest that the clinical picture may be a function both of degree of depression and of ego strength (ability to cope with disturbance under stress). The degree of depression

needed to produce a clinically psychotic picture would thus be less where ego strength is low than where it is high. *J. L. Standen*

1562. **Environmental Change and Age of Onset of Psychosis in Elderly Patients**
C. Buck, J. M. Wanklin, and G. E. Hobbs. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 619–623, June, 1956. 8 refs.

It is suggested that organic psychoses of the senile and arteriosclerotic types may be influenced also by social and psychological factors. Of 516 patients over 64 years of age in mental hospitals in Ontario, 245 were selected because they had experienced a change in environment before the onset of the mental disorder—for example, retirement, a change in the area of residence, a change in living arrangements, or a combination of these. The patients were divided into three groups according to the diagnosis: (1) senile psychosis, (2) arteriosclerotic psychosis, and (3) affective disorders, schizophrenia, and other psychoses. By statistical means, which are outlined, the expected age at onset of psychosis was determined for each group and compared with the observed age at onset, the mean difference being then examined for significance. Among males, the association between change in area, coupled with retirement or with retirement and a change in home situation, and an early onset of disease appeared to be significant. Contrary to expectation retirement alone was not significant. Among females, the effects of changes of area and of the home situation were both significant. In both males and females two environmental changes had more effect than either separately. Women seemed more susceptible to an alteration in domestic environment than to a community one. Breakdown by diagnosis, although resulting in small groups, suggested that these relationships applied to all groups, including the organic psychoses. [As the patients were specially selected the effect of such environmental changes in determining the onset of mental disorder in the elderly cannot be assessed from these results.] *J. N. Agate*

1563. **A New Drug for the Treatment of Alcoholism**
J. K. W. Ferguson. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 793–795, May 15, 1956.

The author, working at the University of Toronto, describes an investigation aimed at finding a substitute for disulfiram which, by causing less severe or fewer side-effects than the latter, would be more readily taken by patients under treatment for alcoholism. The drug selected was citrated calcium carbimide (C.C.C.; "temposil"). Methods of testing the reactions to this and other similar substances in animals and human subjects are described, and the mode of action of both disulfiram and carbimide is discussed. The experiments led to the preparation of a special "slow release" tablet containing 50 mg. of citrated calcium carbimide which, for most cases, is considered to be an effective daily dose satisfying the objects of the research. [For the results of clinical trials of this drug see Abstracts 1564 and 1565.] *R. J. Matthews*

1564. **A New Protective Drug in the Treatment of Alcoholism. (Preliminary Clinical Trial of Citrated Calcium Carbimide)**
J. D. Armstrong and H. T. Kerr. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 795–797, May 15, 1956. 1 ref.

In a study carried out at the Brookside Clinic, Alcoholism Research Foundation, Toronto, to compare the side-effects of citrated calcium carbimide (C.C.C.) [see Abstract 1563] with those of disulfiram in the treatment of alcoholism, 6 out-patients were given C.C.C. in doses of 100 mg. daily for periods of 6 to 25 days, while 13 others received 50 mg. daily for various periods. 10 out of the 19 being treated for at least 21 days. The number and severity of the side-effects were compared with those observed in 33 cases treated with disulfiram in doses of 250 to 500 mg. daily. Of those taking disulfiram only 17 continued to attend for observation after the first few days, whereas more than half of those taking C.C.C. continued attendance for more than 3 weeks. The significance of these facts is discussed. Of the patients taking C.C.C., 7 had previously received disulfiram and had complained of drowsiness, nausea, impotence, or the unpleasant taste, but none complained of these symptoms while receiving C.C.C., and 2 of them said they felt in better health than usual. The authors conclude that C.C.C. appears to produce fewer side-effects than disulfiram. *R. J. Matthews*

1565. **Clinical Trial of Citrated Calcium Carbimide**
R. G. Bell. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 797–798, May 15, 1956.

The author describes the results obtained in 64 alcoholic patients (51 men and 13 women) treated with citrated calcium carbimide (C.C.C.) [see Abstracts 1563 and 1564] at the Bell Clinic, Willowdale, Ontario, between November, 1955, and March, 1956. Of these patients, 24 had previously been treated with disulfiram, and 23 of them had suffered from side-effects, such as weakness, drowsiness, unpleasant taste, body odour, and impotence. The new treatment, which consisted in 50 mg. of C.C.C. given orally in one dose daily, produced none of these complications. The reaction of the drug with test doses of alcohol proved similar to that of disulfiram. C.C.C. provided more rapid—almost instantaneous—protection, but since it was eliminated more rapidly, its duration of action was shorter than that of disulfiram.

The author concludes that C.C.C. is less toxic than disulfiram and, being better tolerated by patients, is more likely to be accepted by them for a period long enough to ensure rehabilitation. He considers also that, if alcohol is taken, there will be fewer delayed or dangerous reactions with the new drug than with disulfiram.

[No details are given of the end-results or relapse rate in these patients, but the test period is too short for these to have much significance. The inference is that most of them were still under observation at least at the end of the period surveyed (March 12, 1956), which may be regarded as a favourable sign.] *R. J. Matthews*

1566. **Treatment of Acute Alcoholism with "Promazine" ("Sparine")**

E. H. MITCHELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 44–45, May 5, 1956. 9 refs.

"Promazine" (10-(3-dimethylaminopropyl)-phenothiazine hydrochloride) was given to 141 patients admitted to the Kalorama Institute, Washington, D.C., for acute alcoholic intoxication. Various complications, chiefly acute alcoholic gastritis and cirrhosis of the liver, were present in 98. In all cases alcohol was withheld and vitamins were administered. The drug was given in a dosage of 25 to 100 mg. every 4 to 6 hours, preferably by mouth, for 3 to 5 days. In some cases 30 to 60 mg. of "butabarbital sodium" was combined with the promazine. There was rapid relief of alcohol-withdrawal symptoms, and in most cases it was possible to give fluids and food after the initial dose. Tremor and agitation were well controlled and the symptoms of gastritis were satisfactorily relieved. The severe anxiety and depressive symptoms, which were observed in 23 patients, were partially relieved. There were no deaths or serious complications. Dizziness occurred in 8% and syncope in 1·5%—mostly in older patients. There was little local reaction to intramuscular injection of promazine in those cases in which vomiting prevented oral administration of the drug. *L. G. Kiloh*

1567. **Management of Acutely Disturbed Patients with Promazine (Sparine)**

J. F. FAZEKAS, J. D. SCHULTZ, P. D. SULLIVAN, and J. G. SHEA. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 46–49, May 5, 1956. 5 refs.

At the District of Columbia General Hospital, Washington, "promazine" was tried in the management of 407 acutely disturbed patients. In a group of 262 patients suffering from acute alcoholic states, including 110 with delirium tremens, the initial dose was 50 to 200 mg. orally, intramuscularly, or intravenously as indicated, and the maintenance dose 50 to 150 mg. 4- or 6-hourly for 4 to 7 days. Usually the patients fell asleep and were maintained subsequently in a quiescent, detached state. Pentobarbitone potentiated the action of promazine and a combination of the two drugs was effective when promazine alone had no influence on the condition. In 3 cases delirium tremens recurred during the course of treatment. There were 2 deaths in this group. The duration of treatment was unaffected by promazine, but patients were more easily managed.

In a group of 103 acutely disturbed, psychotic patients the initial dose of promazine ranged from 50 to 400 mg. Symptoms were well controlled, although in some cases as much as 1·2 g. daily for 7 days was necessary for success. The basic psychosis was unaffected, but the patients were no longer disturbed by their symptoms. Drug-withdrawal symptoms responded satisfactorily to promazine alone in 41 out of 42 patients; only one patient in this group—a heroin addict—did not respond.

Tachycardia and orthostatic hypotension after injection of promazine were infrequent and there were no serious complications. *L. G. Kiloh*

1568. **Experience with the Use of Chlorpromazine and Reserpine in Psychiatry: with Especial Reference to the Significance and Management of Extrapyramidal Dysfunction**

G. W. BROOKS. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1119–1123, June 14, 1956. 2 refs.

The author reports his experience at Vermont State Hospital, Waterbury, with "tranquilizing" drugs in the treatment of 386 female patients with various psychiatric disorders, 187 of whom received chiefly chlorpromazine, 67 chiefly reserpine, and 132 a combination of these two drugs.

Although subject to considerable variation, the usual daily dosage of chlorpromazine was 300 mg. and of reserpine 3 mg., or 150 mg. of the former and 1 mg. of the latter when given together, the duration of treatment ranging from 1 to 16 months. The patients, most of whom presented some problem of disturbed behaviour, included 226 who were suffering from schizophrenia, 30 from manic reaction, 17 from psychoneurosis, 55 from "chronic brain syndrome", and 21 from depression. Treatment had to be discontinued in a small number of cases owing to side-effects.

In general it was found that acute reactions responded more readily than chronic. Of 164 schizophrenics who had been ill 5 years or more, it was possible to discharge 42 (of whom 10 had had deep insulin and most others some electric convulsion therapy) and 73 others were greatly improved, while all but 3 of the remainder became quiet, tractable, and cooperative. On the other hand 40 out of 50 schizophrenics who had been ill less than 5 years were discharged and 7 greatly improved. The facilitation of communication with patients in the former group was particularly impressive. The drugs seemed to have a specific effect in acute manic reactions, but the results in cases of chronic mania were disappointing. They were of considerable value in controlling anxiety, agitation, and acute delirious reactions due to electric convulsion therapy in depressives. The response in cases of chronic brain syndrome was less good. Altogether 151 patients were discharged as a result of treatment, 109 of whom received chiefly chlorpromazine, 15 reserpine only, and 27 both drugs, while 36 failed to respond or were unable to complete the course of treatment. Of those discharged, 51 continued treatment as out-patients. Conditions within the hospital have been "significantly improved" by the introduction of these drugs, and "disturbed wards have been virtually eliminated".

In addition to the usual side-effects of the two drugs, minimal signs of extrapyramidal disorder were detected in 204 cases, usually followed shortly by the initial signs of improvement in the psychosis. These phenomena occurred with both drugs, and particularly when they were given in combination, but were counteracted by giving 5 to 15 mg. of trihexyphenidyl or 3 to 120 mg. of methylphenidyl acetate daily. It was noted that the patients' progress was enhanced when extrapyramidal dysfunction was relieved and the author considers that careful attention to this point contributed greatly to the favourable results obtained. *John C. Kenna*

Dermatology

1569. **Topical Use of Chlorquinaldol**
H. M. ROBINSON and M. B. HOLLANDER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **26**, 143–147, Feb., 1956 [received May, 1956]. 10 refs.

In order to determine the value of chlorquinaldol, an oxyquinoline derivative, in dermatological therapy the drug was tried, incorporated either in an oily-base ointment or in a greaseless-base cream, in the treatment of 756 patients of all ages suffering from 10 different pyogenic and 26 non-pyogenic skin disorders. In this report from the University of Maryland School of Medicine, Baltimore, the results obtained are described and presented in a series of tables [for which the original paper should be consulted].

In general, the authors conclude that chlorquinaldol is of value in a considerable number of the dermatoses, in particular, impetigo contagiosa, infectious eczematoid dermatitis, and paronychia, but is of no value in the treatment of herpes zoster, tinea capitis, acne vulgaris, and some 12 other conditions. Reactions of specific sensitivity were noted in 5 patients.

G. B. Mitchell-Heggs

1570. **The Penetration and Distribution of C^{14}-Hydrocortisone in Human Skin after its Topical Application**
A. SCOTT and F. KALZ. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **26**, 149–158, Feb., 1956 [received May, 1956]. 5 figs., 5 refs.

By means of autoradiography the authors have studied, at McGill University, Montreal, the distribution and penetration of hydrocortisone (labelled with radioactive carbon) into the human skin after topical application in an ointment. In particular they studied: (1) the mode of absorption of hydrocortisone, including the site and rate, and (2) the influence of: (*a*) thickness of the skin, (*b*) pretreatment of the skin with ultraviolet or Grenz irradiation, and (*c*) the type of vehicle. Skin biopsies were performed at intervals in all cases. Penetration of the hormone into the cutis after temporary concentration in the basal layers of the epidermis was demonstrated. It was retarded by thickening of the skin and increased immediately after irradiation, but was not affected by the type of vehicle.

G. B. Mitchell-Heggs

1571. **Novobiocin Treatment of Pyodermas**
J. F. MULLINS and C. J. WILSON. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 201–204, April, 1956. 9 refs.

Novobiocin, a new antibiotic of low toxicity produced by the actinomycete *Streptomyces niveus*, was given at the University of Texas School of Medicine, Galveston, to 30 patients with pyogenic skin infections (mostly impetiginized dermatitis). The dosage of the drug, which was taken by mouth, ranged from 1 to 2 g. daily. "Excellent" results were obtained in 24 cases and "good" results in 3; in one case of inguinal hidradenitis and 2 cases of pustular bacterid the antibiotic was ineffective. No side-reactions were observed.

E. W. Prosser Thomas

1572. **Allergic Eczematous Contact Dermatitis Due to Metallic Nickel**
A. A. FISHER and A. SHAPIRO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 717–721, June 23, 1956. 12 refs.

The authors state that, next to *para*phenylenediamine, nickel is the commonest cause of sensitization dermatitis among patients seen at the Skin and Cancer Unit of the University Hospital, New York. In a review of 198 cases seen over a recent 5-year period the authors stress the part played by intimate contact of nickel objects with the skin, and the importance of friction and of sweating in determining the occurrence of eruptions. They also indicate a number of ways in which the closeness of contact with the metal can be reduced, as by the use of talcum powder. In a re-examination of 40 cases after varying periods it was found that sensitivity to nickel was still present in all but 4 of the patients after periods ranging up to 17 years. They suggest that the 10% solution of nickel sulphate usually used for routine testing purposes is too strong and propose 5% as a more desirable strength. Simultaneous sensitivity to cobalt was found in only 2 cases, and to chrome or copper in none.

It is pointed out that nickel coins are a potential source of aggravation in such patients.

John T. Ingram

1573. **The Juvenile Melanoma of Spitz.** (Le mélanome juvénile de Spitz)
F. WORINGER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1723–1727, May 20, 1956. 9 figs., 16 refs.

The juvenile melanoma described by Spitz (*Amer. J. Path.*, 1948, **24**, 591; *Abstracts of World Surgery*, 1949, **5**, 69) has only recently been recognized in France, and the present author, writing from the Dermatological Clinic, Strasbourg, reports that on reviewing 7 previous cases in which malignant melanoma was diagnosed in children under 11 years, only one proved to be a true case of this condition, the tumours in 6 cases being juvenile melanomata. Altogether 8 cases of juvenile melanoma are described. In general the author's views are those of Spitz. It is pointed out that the lesions usually grow rapidly for 4 to 6 weeks and then remain stable; they are red rather than brown in the early stages, and correspondingly show on histological examination marked vascular dilatation. In the diagnosis of malignancy evidence of intra-epidermal invasion is of considerable help; in juvenile melanoma growth is directed to the dermis only.

Bernard Lennox

Paediatrics

1574. **Bedwetting. Prevalence among Children Aged 4–7 Years**
J. M. BLOMFIELD and J. W. B. DOUGLAS. *Lancet* [*Lancet*] **1**, 850–852, June 2, 1956. 4 refs.

The authors studied the incidence of enuresis among 4,294 children (2,268 boys and 2,026 girls) who were born in March, 1946, and have been followed up for 10 years. The children were from varying social groups and from all areas of Great Britain. At 6 years of age 2·9% of the children were wet by day (1·8% of boys and 4·1% of girls). At the age of 4¼ years 12·2% of children wetted their beds; this figure fell to 10·3% at 6 years and to 7·3% at 7¼ years. In each age group fewer girls than boys wetted their beds, this sex difference being most marked among children of relatively prosperous parents. The incidence of bed-wetting was lower among sibs of dry children than among sibs of bed-wetters, and was lowest among the children of the well-to-do and of agricultural workers. There was no significant difference between the incidence of bed-wetting among first-born children and that among children of later pregnancies or between the incidence among only children and that among children in large families; nor were there any differences between the various regions of England, Wales and Scotland.

It is suggested that the numbers of bed-wetters could be reduced by changes in upbringing or environment but that further research is necessary before effective preventive action can be taken.

Kathleen M. Lawther

1575. **The Influence of Breast Feeding on Weight Gain in Infants in the First Year**
J. MILLIS. *Journal of Pediatrics* [*J. Pediat.*] **48**, 770–775, June, 1956. 10 refs.

The author has studied the increase in weight during the first year of life of 323 babies born at the Kandang Kerbau Maternity Hospital, Singapore. The infants selected were all of single birth, physically mature, and free from congenital defects, and all were domiciled in the urban area. They were divided into 3 classes: (1) 106 infants of Southern Indian families in poor economic circumstances; (2) 103 infants of Chinese parents, also of poor families; and (3) 114 Chinese infants from families in the middle and upper income groups. These samples were representative of the general hospital population in respect of maternal age and birth rank, birth weight, and length of the infants. At birth the babies were weighed to the nearest ounce (28 g.), further weighing being carried out at home visits, so far as possible at the same time of day, at intervals of 2 weeks up to the 12th week and then every 4 weeks up to one year; the method of feeding was recorded at the same time. The results were subjected to an analysis of variance in order to determine the significance of difference in weight gain due to the factors of birth weight and sex.

It was found that breast-feeding influenced the infant's weight, and that in the poor families (Groups 1 and 2) breast-fed babies showed a significantly greater gain in weight at 24 weeks than those artificially fed. But this lead was not maintained at 52 weeks because of an inadequate diet at weaning. In Group 3, however, breast-feeding resulted in no greater weight gain at 24 weeks than artificial feeding, these infants receiving an adequate weaning diet and general care and hygiene of a higher standard. In this group the artificially-fed males were significantly heavier at one year than breast-fed males.

[Although it is recognized that poor health and failure to gain weight are associated, a high rate of gain does not necessarily run parallel with good nutrition. The findings reported here, although of sociological interest, are therefore difficult to interpret. Only the mean weights for the two sexes in each group are given.]

Pamela Aylett

NEONATAL DISORDERS

1576. **Benign Pharyngeal Erythema and Follicle Formation in the Newborn**
A. L. FLORMAN and M. BERGHER. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 549–554, June, 1956. 3 figs., 6 refs.

The authors describe a benign condition causing a curious appearance in the pharynx of newborn infants, which they found on routine examination in 78 (about 20%) of 347 babies born consecutively over a period of 4 months at the North Shore Hospital, Manhasset, Long Island. The lesion appears on one or both anterior tonsillar pillars, mostly on the second or third day but sometimes as early as the first or as late as the fifth day, and consists of one to 3 discrete, white or yellow, circular, slightly elevated areas 1 mm. in diameter on an erythematous base. These may increase in size and number during the next day, but the elevated areas soon disappear, sometimes leaving shallow ulcers and always a generalized erythema. About 3 days after the onset the pharynx appears normal. None of the babies in which this condition was found had any symptoms.

The possible causes suggested are infection, trauma, and oestrogen withdrawal. Investigations are still in progress, but as no unusual bacteria have been found and virus studies—admittedly rather superficial—having so far yielded no result, the authors consider that the cause is not likely to be an infection. There was no correlation between the use of pharyngeal suction immediately after birth and the occurrence of the lesions, so that a traumatic cause seems unlikely. Examination of

pharyngeal smears made with cotton-wool swabs on glass slides, fixed in alcohol and ether, and stained by the Papanicolaou technique showed in normal babies only old squamous cells with small nuclei and large amounts of cytoplasm, whereas in babies with typical pharyngeal lesions there were in addition clusters of cells with larger nuclei and less cytoplasm, such as occur in the deeper epithelial cells of the pharyngeal mucosa. A resemblance between these cells and the cells seen in vaginal smears taken during oestrogen withdrawal suggested this as the most likely cause. The differential diagnosis is from epithelial pearls (Bohn nodules), which are white or yellow spots occurring in the pharynx and also on the gums and are thought to be retention cysts of mucous glands. These are found in infants one to 2 weeks old, have no underlying erythema, and are stated to occur in 90% of babies, though the authors did not see a single case in their survey.

Although the aetiology of the condition, which the authors name "benign pharyngeal erythema", is unknown, it is suggested that as no symptoms occur there is no need for the treatment or isolation of cases.

A. White Franklin

1577. **Myocarditis in Newborns, Caused by Coxsackie Virus. Clinical and Pathological Data.** [In English]
S. VAN CREVELD and H. DE JAGER. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **187**, 100–112, July–Aug., 1956. 2 figs., 4 refs.

During an epidemic of "summer grippe" lasting 2 months in Amsterdam in 1955, 4 fatal cases of myocarditis were observed in newborn infants. The diagnosis was suggested by a preceding influenza-like febrile illness in 3 of the mothers, which was followed by the sudden onset of dyspnoea, cyanosis, or pallor in their infants. In 2 of the cases there were electrocardiographic abnormalities. Necropsy revealed diffuse interstitial myocarditis and, less constantly, focal inflammation in the liver and brain. In all cases Coxsackie virus of Group B, Type 4, was isolated from the heart muscle.

D. Geraint James

1578. **Myocarditis in Newborns due to Group B Coxsackie Virus. Virus Studies.** [In English]
J. D. VERLINDE, H. A. E. VAN TONGEREN, and A. KRET. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **187**, 113–118, July–Aug., 1956. 2 figs., 4 refs.

The authors report from the Netherlands Institute for Preventive Medicine, Leiden, that Coxsackie virus of Group B, Type 4, was isolated from the heart muscle (and in one case the brain) of 5 newborn infants dying of myocarditis during an epidemic in 1955 in Amsterdam. Aqueous suspensions of heart, brain, and lung tissue were inoculated into day-old suckling mice and into HeLa-cell cultures. The mice developed lesions characteristic of Coxsackie-B infection and the cell cultures showed cytopathogenic effects. These lesions were neutralized by type-specific antisera, and by this means it was shown that the myocardial strain of virus was similar to non-myocardial strains obtained at the same time from infants with pleurodynia and aseptic meningitis. The virus produced fever and transient viraemia in two 6-month-old cynomolgus monkeys, and a fatal myocarditis followed the intramuscular inoculation of a 2-day-old cynomolgus monkey.

D. Geraint James

1579. **Neonatal Umbilicus as a Source of Streptococcal Infections in a Maternity Unit**
J. M. BOISSARD and B. ETON. *British Medical Journal* [*Brit. med. J.*] **2**, 574–576, Sept. 8, 1956. 1 fig., 5 refs.

An outbreak of streptococcal infection in the maternity ward of a hospital in Cambridge is described. Pyrexia due to vaginal infection with *Streptococcus pyogenes* Type 9 developed in a woman on the sixth day of the puerperium; on the same day a midwife who had been working in the ward developed tonsillitis which was caused by the same organism. Swabs from the nose and throat of each member of the ward staff and from the nose, throat, and vagina of the other patients were cultured and proved negative. A common source of infection of the patient and midwife was probable, and swabs were therefore taken from the nose, throat, and umbilicus of each of the infants in the unit. *Strep. pyogenes* Type 9 was cultured from umbilical swabs from 5 out of 20 infants, and also from 4 out of 24 infants who had been discharged. A second mother became infected with this organism 13 days after the start of the outbreak.

It is suggested that an attendant without clinical evidence of illness infected the umbilicus of the infant, and that from this source the infection spread either on the hands or on infected clothes and blankets. Prevention of such infection entails exclusion of nurses, midwives, and visitors who are streptococcal carriers and also special care of the umbilical cord. Once infection is established the infants should be given penicillin systemically and sulphanilamide and proflavine should be applied locally to the umbilicus.

R. M. Todd

1580. **Haemolytic Streptococci on the Neonatal Umbilicus**
W. KWANTES and J. R. E. JAMES. *British Medical Journal* [*Brit. med. J.*] **2**, 576–578, Sept. 8, 1956. 17 refs.

An outbreak of haemolytic streptococcal infection occurred recently in two maternity units in, respectively, Carmarthen and Llanelly. In one unit pyrexia developed in 2 patients on the second day of the puerperium, and *Streptococcus pyogenes* was isolated from the vagina. With one exception, nose and throat swabs from the ward staff and patients were negative on culture, the exception being a throat swab from a patient which yielded *Strep. pyogenes*. Subsequently 3 members of the staff and one infant became infected. Umbilical swabs from 6 infants were positive for *Strep. pyogenes*, *Staphylococcus aureus*, or *Proteus*. In the second unit pyrexia in one patient on the third day of the puerperium was caused by vaginal infection with *Strep. pyogenes* Type 12. Umbilical swabs from all 9 infants in the nursery yielded this organism, which was also isolated from umbilical swabs from 5 infants just discharged from the unit. Investigation showed that the organism could be carried by the infants for as long as 8 weeks.

Finally, the authors studied the bacteriology of the umbilicus of 44 infants born at home. Swabs were

taken on the fourth day of life and cultured, but no Group-A haemolytic streptococci were isolated; other groups of haemolytic streptococci were, however, isolated in 4 instances.

Manifest umbilical infection is extremely rare nowadays, but the authors enter a plea for the inclusion of swabbing of the umbilicus of infants in any routine investigation of puerperal infection in a maternity unit.

R. M. Todd

1581. **The Significance of Hypoglycaemia in the Newborn Infant of the Diabetic Woman**

J. W. FARQUHAR. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 203–211, June, 1956. 2 figs., 15 refs.

In a previous paper (*Arch. Dis. Childh.*, 1954, **29**, 519; *Abstracts of World Medicine*, 1955, **17**, 504) the author reported a study of the changes in the blood sugar level in 32 normal infants during the first 6 hours of life. In some of these infants the level was low, but there was no consistent pattern and in only one did it fall below 40 mg. per 100 ml. In the present paper he discusses the results of an investigation of the blood sugar level in 17 infants of diabetic mothers, out of a total of 90 such infants born in the Simpson Memorial Maternity Pavilion, Edinburgh, since 1948. A characteristic pattern was apparent: the blood sugar level fell from the time of birth, reached a minimum at 1 to 2 hours after delivery, and was rising after a few hours. As this pattern was so constant, the level in other infants in the series was estimated only at birth and at 2 hours after delivery. The incidence of episodes of respiratory difficulty which occur in newborn infants of diabetic mothers did not appear to be related to the amount or rate of fall of the blood sugar concentration or to the absolute value reached. Further, no relationship was observed between neonatal death and hypoglycaemia. Of the 90 infants, 8 died in the neonatal period and necropsy revealed hyperplasia of the pancreatic islets in all of them, and a " very adequate cause for death "—adrenal or intracranial haemorrhage, atelectasis, or hyaline membrane disease—in 7; the remaining patient died from anoxia, the cause of which, however, could not be determined.

The subsequent progress of 74 of the surviving infants was studied, with special reference to intelligence and behaviour. There was some retardation in 4, but the author does not consider that this could be attributed to hypoglycaemia, since the latter occurred in only 2 of the retarded children. He doubts whether any serious significance can be attached to neonatal hypoglycaemia and whether the administration of glucose is either necessary or without risk. *H.-J. B. Galbraith*

1582. **Maternal and Cord Blood. A Comparative Investigation with Reference to Blood Sugar, Serum Proteins, Erythrocyte Sedimentation Rate and Total Serum Lipids.** [In English]

U. FURUHJELM. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **2**, Suppl. 5, 1–75, 1956. 9 figs., bibliography.

CLINICAL PAEDIATRICS

1583. **Management of " Idiopathic " Hypercalcaemia in Infancy**

T. STAPLETON, W. B. MACDONALD, and R. LIGHTWOOD. *Lancet* [*Lancet*] **1**, 932–934, June 16, 1956. 2 figs., 11 refs.

The results of balance studies and the clinical findings in an infant suffering from idiopathic hypercalcaemia are described in this report from St. Mary's Hospital, London. Following treatment with a proprietary low-calcium milk preparation and a cereal of low calcium content the plasma calcium level fell to normal, with subsequent clinical recovery. The blood pressure, which had been raised (170 to 185 mm. Hg systolic), fell to normal and a cardiac murmur which was present disappeared. The authors' criteria for a return to a normal diet are: normal serum calcium and blood urea levels, a steady gain in weight, and a normal serum alkaline-phosphatase level. *Winston Turner*

1584. **Obstructive Hydrocephalus in Childhood**

D. S. GORDON and A. R. TAYLOR. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 191–194, June, 1956. 4 figs., 15 refs.

Obstructive hydrocephalus in childhood may be occasioned by a cerebellar tumour or by some non-neoplastic lesion such as stenosis of the aqueduct or obliteration of the foramina in the fourth ventricular roof. The authors review 23 cases seen at the Royal Victoria Hospital, Belfast—15 of which were due to neoplastic and 8 to non-neoplastic lesions—and attempt to establish clinical criteria for the differentiation of the two groups.

In the neoplastic group the duration of symptoms was less than 6 months in cases of medulloblastoma and from 3 to 18 months in those of astrocytoma [the numbers of cases are not stated]; in the non-neoplastic group symptoms had been present for less than 6 months in 5 out of the 8 cases. Medulloblastoma produced vomiting, sometimes without headache, and gross ataxia of the legs in most cases, while astrocytoma tended to cause unilateral ataxia accompanied by headache and vomiting. In 3 patients suffering from non-neoplastic lesions mental retardation was a feature, in 3 progressive obesity developed, while another patient in this group suffered from bouts of hypersomnolence.

Enlargement of the head was a striking feature in some of the non-neoplastic cases. Patients with hydrocephalus of this type usually look well and may be obese, in contrast to the ill-looking children with medulloblastoma, who have usually lost weight. While papilloedema was present almost invariably in both groups, nystagmus was noted in the majority of the neoplastic cases but was not found in the other group. Ataxia was common in the former group, but was less marked in the non-neoplastic group, except for 2 patients with a coarse tremor of the upper limbs. Radiological examination proved valuable in that in the non-neoplastic cases enlargement of the sella with destruction of the

posterior clinoid processes was invariably observed, whereas no such changes were present in the neoplastic group.

The differentiation of obstructive hydrocephalus from other conditions is discussed and the ventriculographic appearances of aqueduct stenosis and foraminal atresia illustrated. *J. E. A. O'Connell*

1585. **The Fate of Children with Bronchiectasis**
C. STRANG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 630–656, April, 1956. 1 fig., 15 refs.

The results are reported of a follow-up study of 209 children with bronchiectasis (119 girls and 90 boys) who, between 1935 and 1948, were admitted to the Newcastle Regional Thoracic Surgery Centre; all were under 15 years of age on admission. Apart from one patient who had emigrated to Australia, a follow-up examination or report was obtained in all cases in 1950, the average follow-up period for survivors then being 6·4 years (range 2 to 15 years).

The onset in 75% of cases was in the first 5 years of life, mostly following pneumonia or acute bronchitis (often associated with measles or whooping-cough) and in 9 cases following pink disease. In 2 cases the bronchiectasis was temporary. A detailed analysis of the signs and symptoms occurring in this series is given. The bronchiectasis, which had been demonstrated by bronchography in all but 5 cases, was unilateral in 150 cases (unilobar in 50), and bilateral in 59. The shadow of a shrunken lower lobe was present in the plain radiograph in 50 cases. The symptoms in bilateral cases were generally worse, but there was no absolute correlation. Bronchoscopic appearances were normal in 8 out of 190 cases; only in 4 were local lesions observed in the bronchus.

Treatment was medical in 46 cases and surgical in 163. Pneumonectomy was performed in 48 cases, in 17 as a double lobectomy or two-stage pneumonectomy. One death occurred during operation and 5 in the immediate postoperative period. Of the 42 survivors, 14 are regarded as completely cured, 18 are greatly improved and fit for school or employment, 5 slightly improved, 2 without improvement (both asthmatic), and 3 worse; 22 complained of shortness of breath, but some of these were breathless before operation. In 10 cases the second lobectomy was required because of persistent postoperative collapse of the upper lobe. Lobectomy (including segmental resection) was performed in 112 cases, being bilateral in 14. There were 10 postoperative deaths and 5 others 2 to 10 years after operation. Of the 97 survivors, 34 are completely well (although 10 have minimal bronchial dilatation), 38 are greatly improved (8 having dilatation), and 14 are slightly improved, 10 being able to go to school. In 11 cases there has been no improvement, although in 8 of these patients the bronchogram appears normal. [The above figures, quoted from the text, leave 3 patients unaccounted for out of the total of 163 treated surgically. In a table, however, the number of patients treated by lobectomy is given as 114, with 17 deaths, and one patient is shown to have died " following plombe operation ".]

The severity of symptoms before operation generally bore no relation to the final result, and of the 31 patients with fetid sputum, 24 are well. The presence of asthmatic symptoms, however, did appear to affect the outcome, and all 7 patients with frank attacks of asthma have failed to do well after operation. Attention is drawn to the problem of persistence of symptoms in some cases in which the postoperative bronchogram is normal, in contrast to the absence of symptoms in others despite residual bronchial dilatation.

The 46 patients treated medically, mainly by postural drainage, form three groups. Of 10 with bronchiectasis too mild in degree to require operation, 2 are well, 3 greatly and 2 slightly improved, and one not improved. Of 20 patients whose bronchiectasis was considered too severe for surgery (of whom 9 might, under present conditions, have been operated on), 9 died within 5 years, 8 are unchanged, and 3 are somewhat improved. Of 16 patients on whom operation was not permitted, 3 died of acute chest illness within 5 years, one is well, 7 have improved, and 5 are unchanged. *A. White Franklin*

1586. **The Effect of Separation Experiences on Children Given Care Away from Home**
J. G. HOWELLS and J. LAYNG. *Medical Officer* [*Med. Offr*] **95**, 345–347, June 29, 1956. 4 refs.

The mothers of 37 children attending a child psychiatric clinic and those of a control group of 37 healthy children, the average age of the children being less than 7 years, were asked to comment on the general effect on the child of separation from home on each occasion on which this had occurred before the age of 5. [No mention is made of the method of selection of the controls, and no account is taken of differences of age, sex, length of separation, or size of family in analysing the reported effects.] When the separation was not due to admission to hospital many of the children showed no harmful effects and some even appeared to enjoy and benefit from it, whereas the effect of admission to hospital was unfavourable in 70% of cases. However, where harmful psychological and physical effects were observed, these were mostly of a temporary nature. Ill effects were reported somewhat less frequently by the mothers of the neurotic children than by those of the controls, but this may be explained by the poorer standard of mothering in the former group. The question of child care in hospitals is discussed and practical suggestions are made concerning the relationship between nurses and children and the need for a homely atmosphere and frequent visiting to minimize the effects of separation. *David Morris*

Correction.—In Abstract 1042 in the October issue it was implied as the result of an editorial error that the study of the growth and development of premature children reported by Dr. J. W. B. Douglas in the *British Medical Journal* (1956, 1, 1210) was carried out at the University of Edinburgh, where the author now holds an appointment. In fact, this work was part of a survey which is being made by a joint committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health, and the Population Investigation Committee, with the support of the Nuffield Foundation, the board of governors of the Hospital for Sick Children, Great Ormond Street, the Ford Foundation, and a number of regional hospital boards.

Public Health and Industrial Medicine

1587. **Fluoridation of Water Supply. The Norway, Maine, Study**
A. H. GARCELON. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1072–1077, June 7, 1956. 2 figs., 17 refs.

This study was undertaken by the Department of Health of the State of Maine to determine how soon the beneficial effects attributable to fluoridation of the water supply begin to become apparent in the teeth of children. In October, 1952, the public water supply of the town of Norway, Maine, (population 3,800) began to receive a dosage of sodium silicofluoride sufficient to maintain a concentration of 1 part of fluoride per 1,000,000. At the same time dental inspections were carried out on all elementary school-children (aged 6 to 12) receiving this water supply, a total of 345. In April, 1955, the inspection was repeated and the average numbers of decayed, missing, and filled permanent teeth in children of various ages compared with the findings in 1952, the total number examined being 313. The figures showed significant improvement in each age group up to 9 years, ranging from 80% at 6 years to 28% at 9 years. The proportion of children aged 7 who were entirely free of decayed, missing, and filled teeth was about 70% (of 44) in 1955 compared with 20% (of 43) in 1952. Thus the effects of fluoridation were readily discernible within 30 months. Comparisons are made with the results of similar investigations carried out in other parts of the United States and certain differences are noted which, however, do not affect the validity of the present author's main conclusions. *R. J. Matthews*

1588. **Variation in Mortality from Heart Disease. Race, Sex, and Socioeconomic Status**
A. M. LILIENFELD. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **71**, 545–552, June, 1956. 7 refs.

It has been demonstrated by Logan that in England and Wales there is an increasing gradient of mortality from coronary heart disease in males from the lowest to the highest social class, while in females there is a gradient in the reverse direction, whereas mortality from other forms of myocardial degeneration in both sexes decreases with improving social status. In the present paper the author presents a comparable analysis of mortality from heart disease in the city of Baltimore during the 3 years 1949–51.

The number of deaths recorded as due to heart disease during this period was 14,504. From the economic characteristics of the various census districts into which the city is divided the population was classified in five groups, the first being roughly comparable to Social Class V in England and Wales and the fifth to Social Classes I and II combined. The age-adjusted mortality was then calculated for each socio-economic group according to sex and race and the figures compared. There was no consistent pattern of variation in mortality from arteriosclerotic heart disease with social grading, in marked contrast to the trends in England and Wales, although in each group the mortality among whites was higher than among non-whites. The two sets of figures agree, however, in showing a clear-cut decline in mortality from other types of myocardial degeneration with improving social circumstances.

The author discusses possible reasons for the absence in the Baltimore figures of any evidence of the apparent relationship between death rate from coronary disease and social class found in England and Wales. This may be due to different methods of socio-economic classification, to the use of different methods of diagnosing, reporting, and classifying the cause of death, or finally to social and biological factors connected with differences in the diet and habits of the two populations. *R. H. Cawley*

1589. **Improvements in Cancer Survival Rates**
M. H. GRISWOLD, S. J. CUTLER, and H. EISENBERG. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1062–1068, June 7, 1956. 3 figs., 3 refs.

This report from the Connecticut State Department of Health is an analysis of survival rates among cases of malignant neoplasm recorded in the Connecticut Cancer Register during the period 1935–51 inclusive. Of 75,494 such cases, 56,908 were reported by hospitals, the diagnosis being confirmed microscopically in 80% of this number. Extensive information was available in the majority of the hospital cases concerning the site and extent of the disease, of the treatment given (which was surgical in 50% of cases in the earlier years and in 63% from 1947 onwards, while the proportion treated by radio- and chemotherapy decreased from 32 to 22%), and of subsequent follow-up to death or (in cases treated before 1947) for at least 5 years. In the remaining 18,586 cases the only information available was that provided by the death certificate and these cases were therefore omitted from the detailed analysis. For the calculation of survival rates the 17-year period was divided into three parts, 1935–40, 1941–6, and 1947–51, standard actuarial methods being applied in the last group, where the 5-year period was unexpended. Survival was calculated from the date of diagnosis, information concerning the date of onset being regarded as unreliable.

For cancer of all types and sites the 5-year survival rate in males rose from 19% in the first period to 25% in the last, the corresponding figures for females being 25% and 38%. In general, there was a marked increase with the years in the survival rates for cancer of the large intestine, cervix and corpus uteri, prostate, and endocrine glands. The prognosis in cancer of the lung, stomach, and oesophagus on the other hand remained poor, less than 10% of patients surviving 5 years. As

might be expected, mortality was highest in the first year after diagnosis and then diminished rapidly until after 5 years it appeared to be little higher than that of the general population.

[For the detailed and very informative analysis of survival according to sex, primary site, and stage of disease at diagnosis the original paper must be consulted.] *R. J. Matthews*

1590. **Diagnosis of Cancer of Lung and Stomach**
A. McKENZIE. *British Medical Journal* [*Brit. med. J.*] 2, 204–207, July 28, 1956. 2 refs.

Between 1916 and 1920 the average number of deaths assigned to carcinoma of the lung and bronchus in England and Wales was 428 per annum, whereas for the year 1954 this number had risen to 16,331. To discover whether cancer of the lung and bronchus is being over-reported on death certificates a questionary was sent from the General Register Office, London, to the practitioner certifying every second death ascribed to this cause during the month of January, 1955. To 770 inquiries, 654 replies were received, and additional information on diagnostic methods was provided in 634 (82%), and these replies are here analysed. The random sample thus obtained corresponded closely in sex ratio and age distribution to the total registrations in 1953.

Diagnoses made on clinical grounds only and by the practitioner alone were classified as "unsupported", those made after *x*-ray examination or consultation as "corroborated", and those after bronchoscopy, histological examination, surgical operation, or necropsy as "established". The final diagnosis was primary carcinoma of the lung in 616 of the 634 cases; 20 (3·2%) were "unsupported", 240 (37·8%) were "corroborated", and 356 (56·2%) were "established". The confirming method was bronchoscopy in 49% and necropsy in 24%.

In 1953 cancer of the stomach accounted for 18·3% of the male and 15·5% of the female deaths in England and Wales certified as due to malignant tumours. Since the incidence of gastric carcinoma appears to vary not only from country to country but also in different areas within the same country and between the two sexes, the possibility of mistaken diagnosis was investigated by sending a questionary similar to the above to the certifying medical practitioner in respect of every second death reported as due to cancer of the stomach in February, 1955. To 497 such inquiries, 437 replies were received. In 13 cases further inquiry revealed that the original cause as given on the death certificate was either wrong or of very doubtful validity. The diagnosis was classed as "established" in 60% of deaths in males but in less than 40% of those in females, while "unsupported" diagnoses constituted a little over 8% of those in males but 18% in females. In each sex the proportion of "established" diagnoses fell with increasing age; thus, in men under the age of 65, three-quarters were so classified, but only one-quarter of those in men of 75 years and over; the corresponding figures for women were two-thirds and one-seventh.

The author concludes that it seems clear that in cancer of the lung and bronchus the standard of diagnostic technique is high and that this cause of death is not being over-reported on death certificates. The only conclusion that can be drawn from the second inquiry is that the certification of death from stomach cancer is less likely to be accurate among older than among younger persons. *F. T. H. Wood*

1591. **Tuberculosis—the Changing Emphasis**
D. THOMSON. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] 15, 99–108, June, 1956. 2 figs., 18 refs.

Tuberculosis is now by far the most dangerous preventable disease, accounting for 67% of all deaths from infective diseases in England and Wales in 1955, and for 79% of those occurring in the productive years of life between the ages of 15 and 39. The present is a critical time for the control of this disease, for in the past 5 years "the biological balance has turned against the tubercle bacillus to a greater extent than ever before". To ascertain the reasons for this improved trend and so to determine the best means whereby it can be continued the author examines in detail certain epidemiological features of tuberculosis over the past century.

Mortality statistics do not give an accurate indication of the trend of incidence, but they are valuable in assessing long-term progress. Although the fall in mortality has been enormous, from a rate of 3,626 per million in 1855 to 148 per million in 1955, the improvement has not been the same for both sexes. In 1855 the rates were equal, but now the number of deaths in males is almost 3 times higher than in females. Remarkable changes have also occurred in the age distribution of the deaths from tuberculosis. Whereas in the past in both sexes the peak mortality was among young adults, the highest mortality among men is now in the age group 60–69 years, while in women, although the highest mortality is still in the age group 35–39, the relative importance of the older age groups has increased. Notification statistics also give an inaccurate indication of the changing size of the tuberculosis problem, since notification is by no means complete, manifestation of the disease may be delayed, and the illness may be due to superinfection. Moreover, the proportion of milder cases reported has probably increased considerably in recent years. Nevertheless, the fact that the case rate for all forms of tuberculosis is now less than one-third of what it was 40 years ago is significant. More reliable indications of the trend of tuberculous infection might be obtained from regular and repeated tuberculin tests in various age groups and from the radiological examination of whole populations. Although the latter technique has been used by the Medical Research Council in the Rhondda Fach investigation, it is doubtful whether it could be carried out on a more extensive scale. On the other hand an increasing number of children are now tuberculin-tested between the ages of 13 and 14 and should provide a worthwhile current index.

The changing pattern of tuberculosis in England and Wales may be regarded as the result of a great epidemic

wave, coinciding with the Industrial Revolution, which started in the eighteenth century and reached a peak around 1810, the subsequent improvement being related to the various social changes, many of which have affected the two sexes unequally. Further improvement must be based on the detection of the disease at an early stage, when it can now be easily and effectively treated. For this purpose the most important measures should be the examination of contacts and specially susceptible social groups, such as vagrants and old men, the widespread tuberculin testing and possibly B.C.G. vaccination of children, and the correct use of specific chemotherapy.

John Fry

1592. **Problems of Salmonella Food-poisoning**

W. SAVAGE. *British Medical Journal* [*Brit. med. J.*] **2**, 317–323, Aug. 11, 1956. 32 refs.

While compulsory notification, the provision of free and extensive laboratory facilities, and increased awareness on the part of Medical Officers of Health have all contributed towards the enormous increase in the reported incidence of food-poisoning, and particularly of food-poisoning due to salmonellae, in recent years in England and Wales, the author suggests that these factors alone cannot account for this phenomenon. Indeed, if the investigation of contacts of the " sporadic " cases which make up the majority of those notified were carried out more often, the infection might well be shown to be more widespread than it appeared, since many cases are mild, and many salmonella-carriers are symptom-free.

During the past 50 years the number of distinct serotypes in the *Salmonella* group, excluding *S. typhosa*, has increased from 3 to over 300. Among the 9 endogenous and 7 exogenous strains most often isolated from food-poisoning incidents during the 6-year period 1949–54, *S. typhimurium* predominated, accounting for 83% of all strains isolated. On the other hand *S. paratyphi* B does not appear at all in this list. [In 1955, however, in an extensive outbreak north of Nottingham, both *S. paratyphi* B and *S. typhimurium* were isolated, separately or together, from cases of food-poisoning and from symptomless excretors, though there were no clinical cases of paratyphoid fever.]

The salmonellae are not natural saprophytic inhabitants of the intestine of man or animals, but cause disease in a very wide variety of animals, including many used for food. The vehicles of infection in food-poisoning outbreaks are much the same today as they were 30 years ago and are implicated with much the same relative frequency, with the exception that the importance of eggs has increased greatly with the extensive and extending use of bulked eggs imported frozen or in other forms in food manufacture. While the safety of canned food and ice-cream has increased, the effect of changes in food habits and commercial practices is that any outbreak which does result from infection of such products is likely to be much more extensive than formerly. Large numbers of salmonellae appear to be necessary to cause food-poisoning and the suitability of the vehicle as a medium for bacterial multiplication is an important factor to be considered in determining its responsibility for an outbreak. Tracing the path of infection from the animal reservoir to the vehicle is frequently the least rewarding part of an investigation, but there is evidence pointing to an extension of salmonella infections in animals.

Infection from human carriers has probably been given undue prominence as a cause of food-poisoning. Infected persons may continue to excrete salmonellae for many weeks, but in steadily diminishing numbers, and the incidence of chronic carriers is very small. However, with the increased incidence of salmonella infections in animals and man the number of persons who, either as symptomless cases or transitory carriers, are excreting salmonella strains in their faeces must also have risen.

The author attributes the current prevalence of food-poisoning to the fact that " public health action has not kept step with the modern revolution in food habits ". Food preparation is increasingly undertaken in bulk rather than in domestic kitchens, and an ever-increasing proportion of the diet consists of processed meat and other foods which are eaten as bought and not cooked in the home, while bulk-feeding habits add to the risk of widespread infection from a single source. To effect the necessary improvement in standards of hygiene in communal feeding-places and in bulk food production education and exhortation must be backed by adequate reserve powers of enforcement.

J. Cauchi

1593. **Viral Hepatitis: Descriptive Epidemiology Based on Morbidity and Mortality Statistics**

I. L. SHERMAN and H. F. EICHENWALD. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 1049–1069, June, 1956. 7 figs., bibliography.

" Infectious hepatitis, including serum hepatitis," has been a notifiable disease in the U.S.A. since 1952, and this report from the Communicable Disease Center of the U.S. Public Health Service, Atlanta, Georgia, is based on the notifications for the period 1952–4, together with the official mortality statistics for the period 1949–53.

The number of cases reported per 100,000 of the population increased from 11·8 in 1952 to 21·7 in 1953 and to 31·1 in 1954. The maximum incidence occurred in February in 1952, in May in 1953, and in March and April in 1954, the rate generally being low in the summer and increasing in the autumn to its peak in late winter or early spring. In contrast, the death rate showed a fairly uniform monthly distribution, and this difference is considered to suggest that the deaths were largely due to serum hepatitis. [The seasonal mortality data are shown only graphically, and although the rates are very small there is, in the abstracter's opinion, a slight indication in each of the four years of a higher winter mortality.]

The annual case rates are given for each of the three years, 1952, 1953, and 1954, for the various States and the monthly incidence over the whole period is shown graphically for four geographical groups of States. In general, the rates in the south-eastern States were high in

1952 and fell in 1953 while those in neighbouring States increased; by 1954 rates of more than 35 cases per 100,000 occurred in States in all areas. In the four groups of States the seasonal patterns were similar and the authors therefore conclude that although the notification of cases has undoubtedly improved, there was a real increase in the incidence of the condition over the 3-year period. Age morbidity curves for five States in 1953 show the maximum rates to be in the age groups 5–9 and 10–14 years, while in Oregon, in which the rate was high at all ages, there was a secondary peak in the age group 25–29 years.

The numbers of deaths from infective hepatitis in each year from 1949 to 1953 and the average age-specific mortality rates for the whole period in males and females are tabulated. Mortality increased with age, but whereas the rates for females exceeded those for males up to 45 years, at older ages the reverse was true.

E. A. Cheeseman

1594. **Infective Hepatitis in a New Housing Estate**
G. T. Crook. *Medical Officer* [*Med. Offr*] **96**, 6–8, July 6, 1956. 5 figs.

Between September, 1954, and August, 1955, there was an unusually high incidence of acute infective hepatitis among 6,650 persons on a housing estate in Luton, 92 cases being identified, although only 7 were notified. It is believed that the infection was more widespread than these figures suggest, and that there were many non-icteric cases, this suggestion finding support in the relatively low incidence in children under 5 years (at which age there is evidence that non-icteric cases are common, at least in institutional outbreaks). The majority of the patients were school-children; there were 9 adults, 6 of whom were teachers. There was no evidence that water, food, or milk was responsible for the spread of infection, which appeared to be by direct transfer from subject to subject. This was demonstrated in the leisurely spread of infection through four families over a period of 6 months. *H. Stanley Banks*

1595. **A Small Outbreak of Poliomyelitis in an Irish Village**
H. G. Nelson. *Medical Officer* [*Med. Offr*] **96**, 8–9, July 6, 1956. 2 refs.

A small outbreak of poliomyelitis occurred in July and August, 1953, in a village near Dublin with 700 inhabitants, 6 cases being diagnosed, 5 of which were of the paralytic form of the disease. It appeared probable that the first 3 patients, children aged 3, 4, and 6 years, contracted the infection when playing together in a barber's shop, the source of infection being a stranger from outside the village who was in the shop on the suspected date of infection. On this assumption the incubation periods in those 3 cases were 5, 8, and 10 days respectively. One of these patients and a possible carrier infected in the barber's shop were the sources of infection in 2 more cases, the incubation periods being 8 and 9 days, and family contacts of one of these 2 patients were believed to have infected a further patient, the incubation period in that event being about 7 days. The author states that having regard to such factors as the different water and milk supplies of the patients' families and the location of their houses, direct contact, mostly of a close familial nature, must have been responsible for the spread of infection. There was one death, that of a man of 48 with bulbar poliomyelitis. Two of the children had had intramuscular injections of penicillin into the thigh 3 weeks before the onset of symptoms, and in both cases paralysis was most severe in the injected limb. *H. Stanley Banks*

INDUSTRIAL MEDICINE

1596. **Aluminium Pneumoconiosis.** (Die Aluminiumlunge)
G. Barth, W. Frik, and H. Scheidemandel. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 1115–1119, July 13, 1956. 32 refs.

Although the danger of aluminium pneumoconiosis, which was prevalent during the war years among workers in the aluminium–bronze industry, appears to have receded with a return to normal conditions and the provision of more adequate protective measures, the occurrence of 3 recent cases has led the authors to re-examine the causes and course of this disease. Following a brief review of the literature they present the findings, at the University Medical Clinic, Erlangen, in 18 cases, 10 of which were fatal, occurring in workers exposed both before and during the war, as well as the 3 which have developed during the last few years.

In the 10 fatal cases there was uninterrupted progression of the disease, with development of spontaneous pneumothorax in 3. The duration of exposure ranged from one to 8 years, and the period of survival after the end of the war from 6 months to 8 years. The cases of 3 of the 8 survivors are described in detail. The first patient, who had been exposed for 14 years (3 of them being war years), showed his first symptoms, that is, dyspnoea, cough, sputum, lack of appetite, and fatigue, 3 years after the beginning of exposure, and has been under observation for 19 years. Radiologically the lungs have shown striation, reticulation, and later fibrous contraction, with a reduction of vital capacity. The condition gradually progressed during the first 16 years and then became static. The second patient was exposed for only 2 years, the disease becoming static one year after the appearance of symptoms; the *x*-ray picture still shows fibrosis of connective tissue, but the vital capacity has improved. The third patient was also exposed for only 2 years, but at the present time, 17 years later, the disease is still progressing, the most significant feature being fibrosis, accompanied by some hyalinization and emphysema. In the remaining 5 survivors the findings were essentially similar, but in all but one mildly progressive case the disease became static after some years. Only one patient developed tuberculosis.

In the 3 cases recently observed the patients had been employed in the aluminium industry both during and after the war, but differed from the former group in the much longer latent period between the beginning of

exposure and the appearance of symptoms—8, 14, and 15 years respectively, compared with one or 2 years in the majority of those working before and during the war only. It is assumed, therefore, that post-war conditions in the industry have been much improved. All 3 cases showed the typical appearances of a mild aluminium pneumoconiosis, both clinically and radiologically, reticulation being slight. The authors point out that in the post-war manufacture of " pyro powder " for export on a considerable scale, no stearin is added, so that in this branch of the industry there is no sharp distinction between the pre- and post-war conditions. They conclude that although aluminium pneumoconiosis is in general a self-limiting reaction, it is possible that in individual cases even stearinized aluminium dust can cause progressive lesions of the lung.

Ethel Browning

1597. **Chronic Bronchitis, Emphysema, and Bronchial Spasm in Bituminous Coal Workers. An Epidemiologic Study**
J. PEMBERTON. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 529–544, June, 1956. 2 figs., 33 refs.

In a study reported from Harvard School of Public Health, Boston, the incidence respectively of chronic bronchitis, emphysema, and bronchial spasm in a selected sample of 240 miners of bituminous coal, aged 45 to 64 years, was compared with the incidence of these conditions in 238 industrial workers and 131 employees of a large engineering plant. All three conditions were present in 40 (16·6%) of the coal-miners, compared with 4 (1·7%) of the industrial workers and 5 (3·8%) of the engineers. On the other hand none of these conditions was seen in 144 (59·5%) of the coal-miners, 195 (82%) of the industrial workers, and 108 (82·5%) of the engineers. In the author's view the higher incidence of these conditions in the coal-miners compared with the other two groups was " largely occupationally determined " [the incidence was not correlated with the number of years spent underground].

There was no correlation between the radiological evidence of pneumoconiosis and the incidence of these conditions. Thus of the 40 coal-miners with all three, 15 showed no radiological evidence of pneumoconiosis; of the remaining 25, evidence of progressive massive fibrosis was found in 2 only, while in 12 the signs of pneumoconiotic changes were minimal.

Kenneth M. A. Perry

1598. **The Treatment of Parkinsonism due to Manganese.** (К вопросу о лечении марганцового паркинсонизма)
S. L. LEVIN and K. I. SUKHOTINA. *Гигиена и Санитария* [*Gigiena*] 29–33, No. 6, June, 1956. 2 figs., 7 refs.

The kymographic investigation of rapidly repeated voluntary movement in 2 cases of Parkinsonism attributed to manganese poisoning showed that there were three phases—a short period of normal movements, a phase of accelerated movements of diminished amplitude, and a period of cessation of movement, the cycle being repeated. After the administration of the mono-calcium salt of adenosine triphosphoric acid intramuscularly such movements became normal and the Parkinsonian symptoms regressed, the effect being still maintained after 8 to 9 months. *R. Crawford*

1599. **The Use of Calcium Disodium Versenate in the Treatment of Chrome Ulceration of the Skin.** (L'uso del calcium disodium versenate nel trattamento delle ulcerazioni cutanee da cromo)
V. GRIANTI and E. BARTALINI. *Rassegna di medicina industriale* [*Rass. Med. industr.*] **25**, 186–190, May–June, 1956. 11 refs.

The authors describe the ulceration of the skin which occurs in those working with chromic acid or the alkaline chromates and bichromates, and discuss the associated problems of treatment and prevention. These ulcers usually develop on the hands (mostly on the backs of the fingers and in the interdigital clefts), forearms, and sometimes on the dorsum of the foot; they are rounded or oval, about the size of a lentil or pea, are punched out, and have a raised, reddish-blue edge with a thin surrounding erythematous halo, infiltrated and firm.

The authors have recently treated 30 cases of this type of ulceration with a chelating agent, the calcium disodium salt of ethylenediamine tetraacetic acid (EDTA; " versene "), in a strength of 10% in a lanoline base. After preliminary cleansing, the ointment was applied and the lesion bandaged, this procedure being repeated every 24 hours up to a maximum of 10 days; the majority of the patients were allowed to carry on with their work. In cases in which the lesions were complicated by purulent folliculitis, antibiotics and vaccines were given as well. This treatment resulted in cure in all cases, and very much more quickly than with other methods. The authors suggest that the usual preventive measures, such as regular medical and radiological examination, issue of protective clothing and anti-dust masks, and the use of nail and tooth brushes, detergent dentifrices, barrier creams, and a special protective cream (containing the chelating agent) for the nose are also necessary.

[It is somewhat surprising that the treatment of ulceration of the nasal septum receives so little mention. In Britain in 1954 out of 220 notified cases of chrome ulceration there were no less than 66 (30%) with nasal septal ulcer. Unless the Italian technical procedure in this industry is very different a similar percentage of nasal ulceration might have been expected in this study.]

W. K. Dunscombe

1600. **Concerning the So-called Pulmonary Concretions in Patients with Silicosis.** (Über sogenannte Lungensteine bei Silikosekranken)
W. EHRHARDT and F. LEICHER. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **15**, 1–18, 1956. 17 figs., 22 refs.

1601. **Affections of the Cornea in French-polishers.** (Die Augenhornhauterkrankung der Möbelpolierer)
E. SCHMID. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **15**, 37–44, 1956. 1 fig., 12 refs.

Forensic Medicine and Toxicology

1602. **Aminophylline (Theophylline Ethylenediamine) Poisoning in Children**
B. H. WHITE and C. W. DAESCHNER. *Journal of Pediatrics* [*J. Pediat.*] **49**, 262–271, Sept., 1956. 1 fig., 12 refs.

1603. **Jaundice Associated with the Administration of Chlorpromazine**
J. M. GAMBESCIA, J. IMBRIGLIA, P. GALAMAGA, and W. WINKELMAN. *Gastroenterology* [*Gastroenterology*] **30**, 735–751, May, 1956. 9 figs., 5 refs.

The authors report, from Hahnemann Medical College and Hospital, Philadelphia, that out of a total of 700 neuropsychiatric patients who had received chlorpromazine by mouth for 2 weeks or longer (of whom 230 were followed up for 18 months), 13 showed abnormal results in liver function tests and 8 developed jaundice. In these 8 patients (4 men and 4 women) the incidence appeared to be unaffected by sex or age, the range of the latter being 21 to 68 years. In 2 cases the dose of chlorpromazine was 10 mg. three times daily and in the others 25 mg. three times daily.

Needle biopsy examination of the liver in 6 out of the 8 cases demonstrated intrahepatic cholestasis, pericholangiolitis, and eosinophilic infiltration. The initial clinical picture was one of a pre-icteric febrile illness accompanied by chills, malaise, anorexia, and nausea, lasting from one to 6 days, succeeded by clinical jaundice which persisted for 4 days to 2 months. Pruritus in variable degree and mild hepatic tenderness were present, but no lymphadenopathy, splenomegaly, spider naevi, or palmar erythema was noted. The predominant laboratory findings were hyperbilirubinaemia, biliuria, and hyperphosphataemia, which occurred in all the cases. At times hypercholesterolaemia was noted, but the flocculation reactions were generally normal; if the latter were positive, peripheral eosinophilia was a frequent but not invariable accompaniment. The authors suggest that the reaction to chlorpromazine may be one of hypersensitivity which, once present, is provoked by a single dose of the drug.

In treatment, 50 mg. of the antihistaminic " benadryl " (diphenhydramine) intramuscularly every 6 hours for 48 hours was without apparent beneficial effect, and the administration of 2 g. of sodium dehydrocholate intravenously every 6 hours for 36 hours resulted in enlargement of the liver, vomiting, oliguria, and abdominal pain. On the other hand 25 mg. of ACTH in 1,000 ml. of 5% glucose injected over an 8-hour period produced a prompt fall in the serum bilirubin level and in the eosinophil count, and later a fall in the serum alkaline phosphatase content. The condition was also relieved by 25 mg. of cortisone four times daily. It is recommended that these two drugs should be given for at least 30 days to prevent a relapse. The similarity of the condition to infective hepatitis is discussed; the authors point out that clinical jaundice is not always necessarily present, fever, an elevated serum phosphatase level, and eosinophilia being the only indications of its presence. *Norval Taylor*

1604. **The Rotherham Lead-poisoning Outbreak**
E. TRAVERS, J. RENDLE-SHORT, and C. C. HARVEY. *Lancet* [*Lancet*] **2**, 113–116, July 21, 1956. 15 refs.

The outbreak of lead poisoning at Rotherham in 1954 has already been described by Gillet (*Lancet*, 1955, **1**, 1118; *Abstracts of World Medicine*, 1955, **18**, 253). In the present paper the clinical aspects are discussed and a number of cases described. Only children were affected, their ages varying from 11 months to 15 years, and no sign of lead absorption was found in 125 adults from the same households. The outbreak was undoubtedly due to the use as domestic fuel of scrap batteries, but poisoning was by ingestion of the residual ash and not by inhalation of fumes. Ten children were severely affected, 2 of whom died before diagnosis, and details are given of the 5 most severe cases. The findings upon examination of 140 others who appeared likely to have been at hazard are described, signs of lead absorption being found in 50. The diagnosis of lead absorption was established from the following indications. (1) On radiography of the long bones, at the growing ends of the shaft a dense line is visible, or in younger children a broad zone of increased density, due to the presence of closely packed trabeculae containing a lead deposit, this being best seen at the lower end of the femur and upper end of the tibia; hence *x*-ray examination of the knee would suffice as a screening test for the purposes of a rapid, large-scale survey. (2) Anaemia, with diminution both in haemoglobin content and in erythrocyte count. (3) Punctate basophilia, with stippled cells forming 0·02% or more of the erythrocyte count gives positive evidence of lead absorption; the stippling is not due merely to immaturity, but to a specific effect of lead on the cytoplasm and cell membrane. (4) Coproporphyrinuria.

Treatment was with calcium ethylenediaminetetraacetic acid (EDTA) given intravenously in two 5-day courses to a total dose of 12 g. The technique is described and details given of the resulting increase in the urinary excretion of lead in 3 of the cases. In addition, sodium citrate and a high-calcium diet in the form of extra milk and calcium lactate, together with vitamin D, were given to help in the removal of lead from the blood and soft tissues and promote its storage in the bones until fully excreted.

No acute toxic episodes have occurred among 58 cases of lead poisoning or absorption followed up for 11 months, but the possible effect on mental development in the severely affected patients cannot yet be assessed.
M. A. Dobbin Crawford

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The authors describe the ulceration of the skin which occurs in those working with chromic acid or the alkaline chromates and bichromates, and discuss the associated problems of treatment and prevention. These ulcers usually develop on the hands (mostly on the backs of the fingers and in the interdigital clefts), forearms, and sometimes on the dorsum of the foot; they are rounded or oval, about the size of a lentil or pea, are punched out, and have a raised, reddish-blue edge with a thin surrounding erythematous halo, infiltrated and firm.

The authors have recently treated 30 cases of this type of ulceration with a chelating agent, the calcium disodium salt of ethylenediamine tetraacetic acid (EDTA; " versene "), in a strength of 10% in a lanoline base. After preliminary cleansing, the ointment was applied and the lesion bandaged, this procedure being repeated every 24 hours up to a maximum of 10 days; the majority of the patients were allowed to carry on with their work. In cases in which the lesions were complicated by purulent folliculitis, antibiotics and vaccines were given as well. This treatment resulted in cure in all cases, and very much more quickly than with other methods. The authors suggest that the usual preventive measures, such as regular medical and radiological examination, issue of protective clothing and anti-dust masks, and the use of nail and tooth brushes, detergent dentifrices, barrier creams, and a special protective cream (containing the chelating agent) for the nose are also necessary.

[It is somewhat surprising that the treatment of ulceration of the nasal septum receives so little mention. In Britain in 1954 out of 220 notified cases of chrome ulceration there were no less than 66 (30%) with nasal septal ulcer. Unless the Italian technical procedure in this industry is very different a similar percentage of nasal ulceration might have been expected in this study.]

W. K. Dunscombe

1600. **Concerning the So-called Pulmonary Concretions in Patients with Silicosis.** (Über sogenannte Lungensteine bei Silikosekranken)
W. EHRHARDT and F. LEICHER. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **15**, 1–18, 1956. 17 figs., 22 refs.

1601. **Affections of the Cornea in French-polishers.** (Die Augenhornhauterkrankung der Möbelpolierer)
E. SCHMID. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **15**, 37–44, 1956. 1 fig., 12 refs.

Forensic Medicine and Toxicology

1602. **Aminophylline (Theophylline Ethylenediamine) Poisoning in Children**
B. H. WHITE and C. W. DAESCHNER. *Journal of Pediatrics* [*J. Pediat.*] **49**, 262–271, Sept., 1956. 1 fig., 12 refs.

1603. **Jaundice Associated with the Administration of Chlorpromazine**
J. M. GAMBESCIA, J. IMBRIGLIA, P. GALAMAGA, and W. WINKELMAN. *Gastroenterology* [*Gastroenterology*] **30**, 735–751, May, 1956. 9 figs., 5 refs.

The authors report, from Hahnemann Medical College and Hospital, Philadelphia, that out of a total of 700 neuropsychiatric patients who had received chlorpromazine by mouth for 2 weeks or longer (of whom 230 were followed up for 18 months), 13 showed abnormal results in liver function tests and 8 developed jaundice. In these 8 patients (4 men and 4 women) the incidence appeared to be unaffected by sex or age, the range of the latter being 21 to 68 years. In 2 cases the dose of chlorpromazine was 10 mg. three times daily and in the others 25 mg. three times daily.

Needle biopsy examination of the liver in 6 out of the 8 cases demonstrated intrahepatic cholestasis, pericholangiolitis, and eosinophilic infiltration. The initial clinical picture was one of a pre-icteric febrile illness accompanied by chills, malaise, anorexia, and nausea, lasting from one to 6 days, succeeded by clinical jaundice which persisted for 4 days to 2 months. Pruritus in variable degree and mild hepatic tenderness were present, but no lymphadenopathy, splenomegaly, spider naevi, or palmar erythema was noted. The predominant laboratory findings were hyperbilirubinaemia, biliuria, and hyperphosphataemia, which occurred in all the cases. At times hypercholesterolaemia was noted, but the flocculation reactions were generally normal; if the latter were positive, peripheral eosinophilia was a frequent but not invariable accompaniment. The authors suggest that the reaction to chlorpromazine may be one of hypersensitivity which, once present, is provoked by a single dose of the drug.

In treatment, 50 mg. of the antihistaminic " benadryl " (diphenhydramine) intramuscularly every 6 hours for 48 hours was without apparent beneficial effect, and the administration of 2 g. of sodium dehydrocholate intravenously every 6 hours for 36 hours resulted in enlargement of the liver, vomiting, oliguria, and abdominal pain. On the other hand 25 mg. of ACTH in 1,000 ml. of 5% glucose injected over an 8-hour period produced a prompt fall in the serum bilirubin level and in the eosinophil count, and later a fall in the serum alkaline phosphatase content. The condition was also relieved by 25 mg. of cortisone four times daily. It is recommended that these two drugs should be given for at least 30 days to prevent a relapse. The similarity of the condition to infective hepatitis is discussed; the authors point out that clinical jaundice is not always necessarily present, fever, an elevated serum phosphatase level, and eosinophilia being the only indications of its presence. *Norval Taylor*

1604. **The Rotherham Lead-poisoning Outbreak**
E. TRAVERS, J. RENDLE-SHORT, and C. C. HARVEY. *Lancet* [*Lancet*] **2**, 113–116, July 21, 1956. 15 refs.

The outbreak of lead poisoning at Rotherham in 1954 has already been described by Gillet (*Lancet*, 1955, **1**, 1118; *Abstracts of World Medicine*, 1955, **18**, 253). In the present paper the clinical aspects are discussed and a number of cases described. Only children were affected, their ages varying from 11 months to 15 years, and no sign of lead absorption was found in 125 adults from the same households. The outbreak was undoubtedly due to the use as domestic fuel of scrap batteries, but poisoning was by ingestion of the residual ash and not by inhalation of fumes. Ten children were severely affected, 2 of whom died before diagnosis, and details are given of the 5 most severe cases. The findings upon examination of 140 others who appeared likely to have been at hazard are described, signs of lead absorption being found in 50. The diagnosis of lead absorption was established from the following indications. (1) On radiography of the long bones, at the growing ends of the shaft a dense line is visible, or in younger children a broad zone of increased density, due to the presence of closely packed trabeculae containing a lead deposit, this being best seen at the lower end of the femur and upper end of the tibia; hence *x*-ray examination of the knee would suffice as a screening test for the purposes of a rapid, large-scale survey. (2) Anaemia, with diminution both in haemoglobin content and in erythrocyte count. (3) Punctate basophilia, with stippled cells forming 0·02% or more of the erythrocyte count gives positive evidence of lead absorption; the stippling is not due merely to immaturity, but to a specific effect of lead on the cytoplasm and cell membrane. (4) Coproporphyrinuria.

Treatment was with calcium ethylenediaminetetraacetic acid (EDTA) given intravenously in two 5-day courses to a total dose of 12 g. The technique is described and details given of the resulting increase in the urinary excretion of lead in 3 of the cases. In addition, sodium citrate and a high-calcium diet in the form of extra milk and calcium lactate, together with vitamin D, were given to help in the removal of lead from the blood and soft tissues and promote its storage in the bones until fully excreted.

No acute toxic episodes have occurred among 58 cases of lead poisoning or absorption followed up for 11 months, but the possible effect on mental development in the severely affected patients cannot yet be assessed.
M. A. Dobbin Crawford

Anaesthetics

1605. **Observations on Steroid Anaesthesia. A Preliminary Report**
R. P. HARBORD and W. N. WILD. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **49**, 487–492, July, 1956. 6 figs., 5 refs.

Deep anaesthesia has been obtained with large doses of steroid hormones. Selye (*Endocrinology*, 1942, **30**, 437) used the intraperitoneal route successfully, but hydroxydione (" viadril ") may be given intravenously, because it is soluble. Some workers, however, have found that hydroxydione in a 2·5% solution is irritating to veins. The present authors quote 4 bad-risk cases in which this drug was given and then describe the results in 25 miscellaneous cases (including 16 subjected to major abdominal surgery). Of the 4 bad-risk patients, one died on the operating table and another 48 hours later. Induction in the authors' series was usually with 0·5 g. of hydroxydione, relaxants being needed for intubation. Hiccup occurred in 9 cases, and hypotension, usually transitory, developed in 5. The postoperative condition of the patients was considered to be better than that observed after other anaesthetics.

The authors considered that the drug depressed respiration, and movement was liable to occur on stimulation. There was a rough correlation between the dose and the period of unconsciousness. Since the steroid showed some tendency to cause thrombosis the authors propose to use weaker solutions in future and to explore the possibility of giving various combinations of other drugs with hydroxydione. *W. Stanley Sykes*

1606. **Viadril: a New Steroid Anaesthetic. Preliminary Communication**
L. H. LERMAN. *British Medical Journal* [*Brit. med. J.*] **2**, 129–132, July 21, 1956. 8 refs.

" Viadril " (21-hydroxypregnane-3:20-dione sodium acetate), a steroid, was the principal anaesthetic agent in 19 cases in which various operations lasting 8 to 90 minutes were performed. Usually premedication was with 22 mg. of " omnopon " and 0.43 mg. of scopolamine. Induction of anaesthesia was by slow injection of a 2·5% solution of viadril into the tubing of a fast-running normal-saline drip; sleep resulted within about 5 minutes, when administration was begun of a mixture of 3 parts of nitrous oxide and one part of oxygen, and maintained throughout anaesthesia. The total amount of viadril required ranged from 500 to 1,250 mg. In almost every case there was adequate relaxation without recourse to muscle relaxants. Analgesics were not necessary. A fall in blood pressure was common, and haemorrhage was usually much reduced. There was early recovery of consciousness; vomiting occurred in only one case. Thrombophlebitis developed in the injected arm in 2 instances. Detailed reports of 3 of the cases are given. *Mark Swerdlow*

1607. **An Intravenous Steroid Anaesthetic. Experiences with " Viadril "**
A. H. GALLEY and M. ROOMS. *Lancet* [*Lancet*] **1**, 990–994, June 23, 1956. 3 figs., 16 refs.

A steroid, " viadril ", which is a derivative of pregnanedione, was the basic anaesthetic in 100 operations carried out at King's College Hospital, London. In order to avoid venous thrombosis the method of administration was by intravenous drip and the strength of the solution was less than 0·5%, a suitable solution for routine use being obtained by dissolving five 500-mg. vials of the drug in the usual 540-ml. bottle of intravenous saline. With a drip rate of 150 a minute the average patient became drowsy within 5 to 7 minutes and fell asleep within 10 minutes, although he could still be roused. After 15 minutes the patient was in a deep sleep but reacted to traumatic stimuli. The authors state that at this stage the patient tolerated a carefully inserted pharyngeal airway and laryngoscopy was possible; the vocal cords were widely abducted, and although they closed when touched, they opened again at once. Intubation was easier than with thiopentone and the tube was much better tolerated in the trachea, with a most satisfactory absence of " bucking ". The long induction period of 20 to 25 minutes could be halved by using the gas–oxygen–pethidine sequence immediately after loss of consciousness.

Doses up to 2 g. of viadril did not appear to affect either the rate or depth of respiration. Circulatory changes were fairly constant, with a marked fall in blood pressure and tachycardia. Sharp falls in blood pressure were encountered irrespective of age, but were much less likely if the drug was given slowly; they were readily controlled, however, by administration of methylamphetamine. The authors consider that viadril has analgesic properties, as evidenced by the absence of changes in respiration or pulse rate during traumatic stimulation.

The after-effects were striking, especially the sense of well-being and the absence of postoperative fatigue. Compared with thiopentone viadril has the disadvantage that the induction time is long, but it gives better conditions for laryngoscopy, thyroidectomy, and major procedures in which intravenous infusions are necessary.

The authors conclude by discussing steroid anaesthesia in relation to the rhythm of sleep, and suggest that normal sleep may be the effect of an autogenous steroid which suppresses the reticulo-activating centre and thus robs the cortex of its normal alarm mechanism.

Michael Kerr

1608. **New Drugs and an Era of Analgesia and Amnesia**
J. S. LUNDY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 97–101, Sept. 8, 1956.

Radiology

1609. **Malignant Disease in Childhood and Diagnostic Irradiation in Utero**
A. STEWART, J. WEBB, D. GILES, and D. HEWITT. *Lancet* [*Lancet*] **2**, 447, Sept. 1, 1956. 5 refs.

Some 1,500 children under the age of 10 years died of leukaemia or malignant disease in England during the years 1953–5, and the Department of Social Medicine of the University of Oxford, in cooperation with Public Health Departments throughout the country, is conducting an environmental survey into these cases. In each case the parents are visited and inquiries made according to a standard schedule, similar inquiries being made concerning a control child of the same age and sex selected at random from among those born in the same area. The present paper is a preliminary communication analysing the data collected so far (representing about one-third of the cases).

In 42 of the 269 cases of leukaemia studied the mother had undergone diagnostic radiography of the abdomen during pregnancy, compared with only 24 in the control group. Similarly there was a history of antenatal radiography in 43 out of 278 cases of other forms of malignant disease as against 21 in the control group. There was, however, no marked difference between the mothers of affected children and the controls in the number of *x*-ray examinations carried out during pregnancy on other parts of the body or of examinations made before conception or after parturition. These findings are held to suggest that children exposed to *x* rays in utero are more prone to develop leukaemia and other malignant diseases than are children who have not received such irradiation.

(In subsequent correspondence (*Lancet*, 1956, **1**, 573) the criticism was made that since it is likely that *x*-ray examinations are made more frequently in the first than in subsequent pregnancies, the authors' conclusion would be fully valid only if the controls were matched for birth rank, which in itself might be related to the aetiology of leukaemia. In reply the senior author stated that had the controls been so matched it would have been impossible to discover what appears to be the case—that children dying of leukaemia and cancer include a disproportionately large number of first-born children and of twins, the other twin being unaffected in several cases, as a result, it is suggested, of screening by the affected twin. Even if information concerning antenatal radiography had not been sought in the first place, this discovery would have suggested that *x* rays were a possible factor.)

[The final report will be awaited with great interest, and in the meantime it would obviously be wise to limit radiation during pregnancy to a minimum and to those cases where the benefit likely to accrue to mother and child from the increased accuracy of diagnosis would outweigh a remoter risk of leukaemia.]

G. Ansell

1610. **Cerebral Angiography in a Neurosurgical Service**
S. DIMANT, C. P. MOXON, and N. A. LEWTAS. *British Medical Journal* [*Brit. med. J.*] **2**, 10–16, July 7, 1956. 1 fig., 19 refs.

The authors review the results of 1,556 carotid angiograms performed on 1,007 patients, nearly half of them in the out-patient department, at Manchester Royal Infirmary between 1950 and 1954, and assess the indications for angiography, the accuracy of the information so obtained, and the discomforts and complications which may result.

In this series 281 patients were shown by means of angiography to have an intracerebral vascular lesion, while in a further 133 cases in which the result of angiography was negative a final diagnosis of vascular disorder was made. In most cases of aneurysm the site of the lesion was accurately shown. The site of angiomata can also be reliably demonstrated, but a large intracerebral clot may cause compression or thrombosis of the fistulous vessels so that only the vascular displacement may be seen. The site of an intracerebral clot was indicated in 13 instances and surgical removal followed. Bilateral carotid angiography was performed at the earliest opportunity in all cases of subarachnoid haemorrhage. Bilateral vertebral angiography should be performed in these cases, but a safe and sure percutaneous technique has not yet been perfected; its use is therefore restricted to cases in which there has been severe and repeated haemorrhage, especially in young patients, and where there is clinical evidence of lesions of the posterior fossa, especially an angioma. In 6 out of 8 cases of angioma demonstrated by vertebral angiography carotid angiography also revealed the lesion in each case.

Angiography, however, is not regarded as a proper substitute for bilateral burr-hole exploration in cases of subdural haematoma owing to the ease with which anterior clots can be overlooked. In cases in which it is difficult to distinguish vascular disease from brain tumour, angiography may be extremely helpful. On the other hand, the procedure may precipitate spasm and thrombosis in diseased vessels and thus endanger an already precarious collateral circulation. In addition, diodone may cause cerebral oedema and involve comparatively ischaemic areas. It is concluded that angiography is a relatively safe and reliable method of demonstrating brain tumour, in many cases revealing vascular patterns which provide specific evidence of the pathology. When the intracranial tension is high, angiography is a safer investigation than encephalography or pneumoventriculography. Angiography, however, is an unreliable method, as compared with pneumoencephalography, for the demonstration of cerebral atrophy. The repetition of angiograms in follow-up studies after operation is of value in showing the degree of obliterations of an aneurysm, the fate of arterio-venous fistulae, the extent of tumour removal, and early signs of recur-

rence. The procedure can be carried out in the out-patient department, many patients being unaffected and ready to go home within an hour, although others may suffer pain and anxiety which leave them exhausted for some hours. In regard to complications, the chief cause of overnight admission in 5% of out-patients was distension of the neck by a haematoma. Large haematomata causing increasing dyspnoea are rare but, when they occur, call for urgent laryngeal intubation. The mortality in the present series was 0·2%.

John H. L. Conway-Hughes

1611. **Temporary Arrest of the Contrast Medium in Angiocardiography.** [In English]
A. Celis, R. Cicero, H. Del Castillo, and E. Arce. *Acta radiologica* [*Acta radiol. (Stockh.)*] **45**, 341–351, May, 1956. 11 figs., 17 refs.

When opaque medium is injected into the superior vena cava above the azygos arch it diffuses in the same direction as the blood flow because of the negative intrathoracic pressure. If, however, this pressure is made positive by the Valsalva manœuvre the circulation of the blood may then be arrested. At the Hospital General, Mexico City, the angiocardiographic findings during this manœuvre were studied in 58 persons who were healthy from the cardiovascular point of view.

The manœuvre produced a reduction in the calibre of the superior vena cava, its outline was undulating, its tributaries were rendered opaque, there was filling of the veins of the neck, and the progression of the contrast medium was considerably slowed. In the heart the right atrium was diminished in size and its margins sharply defined, the auricular surface of the tricuspid valve being represented by a straight line. Isolated visualization of the right ventricle could be obtained if the tip of the catheter was introduced into this chamber, the volume of which was diminished in size. In some cases the pulmonary artery was seen simultaneously with the ventricle, but with less contrast. Variations in the volume of the main pulmonary artery were observed, its diameter being increased and the sigmoid valves closed. It was not possible to obtain simultaneous visualization of the arteries and veins in the lungs. The inferior vena cava showed an undulating outline and some filling of its tributaries.

An examination of 1,222 angiocardiograms carried out in the usual manner revealed that only in cases of bronchogenic carcinoma was the azygos vein outlined, suggesting that this vein is visualized only in cases in which the superior vena cava is obstructed.

John H. L. Conway-Hughes

1612. **Intravenous Cholangio-cholecystography.** (Внутривенная холангио-холецистография)
E. M. Kagan and I. A. Shekhter. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 43–49, No. 5, May, 1956. 8 figs., 6 refs.

This article from the Institute of Roentgenology, Moscow, describes a method of intravenous cholangiography with a new contrast medium, " bilignost ". This product, the structural formula of which is given, contains 64·38% of iodine. It is used in a 20% solution, with a *p*H of 5·49, a dose of 30 to 40 ml. being injected over a period of 3 to 4 minutes; if it is given more rapidly, nausea and a tendency to vomit may occur, but these pass off in a few minutes. The dye appears in the biliary duct within 10 to 15 minutes, and in the gall-bladder in 45 minutes; the shadow of the gall-bladder reaches its maximum intensity in 90 to 120 minutes after injection.

Bilignost is very slightly toxic, the mean lethal dose being 3·4 g. per kg. body weight, as against 0·3 g. for " bilitrast " or " biliselectan ", but severe reactions are rare. The authors recommend, however, that it should be employed only after a test dose of 1 or 2 ml. injected intravenously has excluded the presence of iodine sensitivity. Apart from this, no special preparation of the patient is necessary.

(The paper includes 6 excellent reproductions of radiographs and 2 diagrams.) *L. Firman-Edwards*

1613. **Delayed Effects Occurring within the First Decade after Exposure of Young Individuals to the Hiroshima Atomic Bomb**
R. W. Miller. *Pediatrics* [*Pediatrics*] **18**, 1–18, July, 1956. 1 fig., 41 refs.

The first atomic bomb was dropped on Hiroshima in August, 1945. Previous studies of its effects are briefly reviewed, and the latest findings up to the beginning of 1955 are reported. The aim was to examine all survivors; at the time of detonation the youngest were in utero and the oldest were 10 years of age. A total of 4,407 patients were seen, of whom 2,771 were 19 years old or less in 1954 and were within 3,000 metres of the hypocentre (the point directly under the bomb). Significant amounts of radiation are believed to have been received up to a distance of 1,800 metres.

Among 159 who were in utero in 1945 there were 33 cases of microcephaly; 24 of these patients were exposed at an estimated gestational age of 7 to 15 weeks, which seemed to be the period of greatest susceptibility. Of these 33 patients, 15 also showed mental retardation. Both microcephaly and mental retardation were directly related, in incidence and severity, to nearness to the hypocentre; in most of the cases showing both effects the mothers had been within 1,500 metres. No other embryological effects were noted. In the 6 years 1949 to 1954, 19 patients under the age of 19 who had been within 2,100 metres of the hypocentre developed leukaemia, an incidence over 10 times as high as that in those at greater distances; in 7 cases the leukaemia was of granulocytic type, in 7 lymphocytic, and in 5 uncertain; no age group was specially susceptible. There was no evidence of aplastic anaemia or other blood dyscrasias. No cases of cataract sufficient to disturb vision were found, though occasional small opacities were observed on ophthalmoscopy. Some mild visual disability was found in patients exposed at under 1,800 metres, but its cause is uncertain. No increased tumour incidence (apart from the leukaemia) and no increased susceptibility to infection (taking the incidence of chronic otitis media as the criterion) were observed. Evidence for a possible premature ageing effect remains to be gathered later. Among the survivors the fear of late

effects was common and is considered to be potentially disabling in some cases. Lesions due to blast or burns were noted in 24 cases, and included osteomyelitis, eye abnormalities, paralysis, deforming scars, and the presence of foreign bodies. *J. Walter*

1614. **Radio-yttrium (Y^{90}) for the Palliative Treatment of Effusions Due to Malignancy**
E. P. SIEGEL, H. E. HART, M. BROTHERS, H. SPENCER, and D. LASZLO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 499–503, June 9, 1956. 2 figs., 9 refs.

Radioactive yttrium (^{90}Y) has been used by the authors at the Montefiore Hospital, New York, in the palliative treatment of patients with pleural and peritoneal effusions due to malignant disease. Since the isotope is a pure β-ray emitter with a half-life of 61 hours it requires only moderate shielding and " presents no hazard " to medical and nursing staff. It is introduced into the cavity in the presence of sufficient yttrium carrier. Localization of ^{90}Y, due probably to the formation of colloids of yttrium with the constituents of the fluid, mainly protein, has been reported. The authors therefore dilute the isotope with some of the aspirated fluid before injection. Examination of the blood, urine, and faeces after injection showed that the amount of radioactivity in the blood was not significant and that in the urine and faeces very low.

Of 16 patients selected for treatment because they had previously required repeated aspiration, 13 received ^{90}Y intrapleurally and 3 intraperitoneally. Of the former group 7 benefited, the dosage being 10 to 30 millicuries; of the patients given the isotope intraperitoneally one was considerably improved, the dosage in this instance being 40 millicuries.

There appeared to be no side-effects and no radiation sickness. The results suggest that this method may find a place in the palliative management of cases of carcinoma with effusion. *M. P. Cole*

1615. **Cancer of the Thyroid and Irradiation**
E. M. UHLMANN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 504–507, June 9, 1956. 13 refs.

The author discusses the recent increase in the incidence of carcinoma of the thyroid gland in children and the possible relationship between this increase and previous therapeutic irradiation of the head and neck, as postulated by Clark (*J. Amer. med. Ass.*, 1955, **159**, 1007; *Abstracts of World Medicine*, 1956, **19**, 412). From a review of the literature he concludes that there is no evidence of such a relationship and brings various arguments to bear against the hypothesis.

He then reports his own observations at the Michael Reese Hospital, Chicago, on a series of 25 cases of thyroid cancer occurring in persons under the age of 21. Of these, only 4 had had any previous *x*-ray treatment, and in these 4 cases the intervals between the irradiation and the development of malignancy were 8, 9, 14, and 15 years respectively. Moreover, during a follow-up study covering periods up to 7 years not one case of thyroid cancer occurred among 480 children who had received *x*-ray treatment for enlarged tonsils and adenoids. The maximum skin dose delivered over the thyroid gland in the course of *x*-ray treatment for hypertrophic lymphoid tissue in the pharynx and tonsil in a typical case is shown to be 18 r over a period of 2 weeks. This figure is exceeded by a considerable margin in the fluoroscopic examination of the chest, so that a much higher incidence of thyroid cancer might reasonably be expected if irradiation were a cause of its development. *H. C. Warrington*

1616. **Clinical Considerations in the Isotope Treatment of Carcinoma of the Digestive Tract.** (Klinische Betrachtungen zur Isotopenbehandlung der Karzinome des Verdauungstraktes)
J. BECKER and K. E. SCHEER. *Strahlentherapie* [*Strahlentherapie*] **100**, 184–191, 1956. 7 figs., 10 refs.

In the treatment of carcinoma the use of radioactive isotopes provides an improved method of palliation, often in conjunction with external radiation, which is well exemplified in tumours of the digestive tract. For the tongue the following may be used: needles or wire of tantalum, cobalt, or gold, intravascular particles of gold or phosphorus, and interstitial colloidal or crystalline gold or phosphorus. In the oesophagus a long intracavitary chain of radioactive cobalt " pearls " gives better depth-dosage than does radium, and there is less tendency to stenosis than with external radiation alone. A surface dose of 3,000 r is given, followed by rotation therapy (5,000 to 6,000 r in 30 sessions) and then 3,000 r by cobalt pearls, immediately or after an interval of 8 weeks. A proliferative growth can be infiltrated with phosphorus or gold through the oesophagoscope.

For gastric carcinoma teleradium therapy is preferred, especially for growths near the cardia. Intracavitary contact therapy through a gastrostomy is useful, if the general condition of the patient allows; balloons are inserted and filled with radioactive solutions or " macrosuspensions ", that is, tiny radioactive particles in viscous fluid, giving 6,000 r at the surface in two applications. For inoperable growths of the small intestine and colon, telecobalt therapy may be used. For those of the rectum and sigmoid colon the conditions are more favourable after colostomy; needles or wire of tantalum, cobalt, or gold may be used at the operation, or inserted through a proctoscope. Rubber balloons (as described above) are also very useful, 8,000 r being given in three applications. The best results are in rectal growths, and some apparently inoperable cases may be rendered operable. For metastases in the liver the intravenous injection of suitably sized radioactive particles may help, as 50 to 60% of these are concentrated in the liver, although the highest dose unfortunately goes to normal liver tissue. Isolated metastases on the surface of the liver can be infiltrated with gold. Lymph nodes take up radioactive colloids injected intraperitoneally, but only if the lymphatic channels are not blocked; nodes completely replaced by neoplastic growth cannot therefore be reached. Ascites, however, can be controlled, with abolition of protein loss and prolongation of life. *J. Walter*

History of Medicine

1617. **The Cholera, 1831**
C. F. BROCKINGTON. *Medical Officer* [*Med. Offr*] **96**, 75, Aug. 10, 1956.

In reviewing briefly the spread of cholera from India to its appearance in England in 1831, the author draws attention to the formation of two Boards of Health in London. With preparedness as its watchword, a Board was formed at the Royal College of Physicians in January, 1831. This Board, after examining seven medical men with previous experience of cholera in India, issued a long report in August to guide practitioners in the recognition of the early symptoms of the disease, a supplement being issued in October. In the same month, by an Order in Council, attention was drawn to the dangers of the disease reaching the shores of England by illicit intercourse with the European Continent where the disease raged, and a recommendation was made that every town and village, especially coastal ones, set up local boards of health, with suitable medical representation on them, one of the doctors to act as correspondent with the Board in London. Thus the earliest information could be obtained as to when and where the cholera first appeared. Later, a circular was issued to the chairmen of the local boards of health giving more detailed instructions as to organization and reporting to the London Board.

Towards the end of the year the government established a Central Board of Health at Whitehall which worked alongside the Board set up at the College. Cholera first appeared in England at Sunderland in November, 1831, and its occurrence in London was first announced in the *Gazette* in February, 1832. A further Order in Council, issued on February 29, 1832, required all established boards in England and Wales to remain in operation and to execute their duties concerning the disease, and every practitioner was required to make to his local board a daily report of all new cases of, and deaths and recoveries from, cholera or " any other disease anywise resembling the same ". The *Cholera Gazette* appeared on January 14, 1832, and during this first outbreak in England many physicians wrote good accounts of the disease.

Such records as have survived of this early venture in setting up boards of health suggest that it was a well-thought-out plan, but it is not known how widely it was extended. *H. P. Tait*

1618. **Benevenutus Grassus**
A. SCHLOSSMAN. *Eye, Ear, Nose and Throat Monthly* [*Eye, Ear, Nose Thr. Monthly*] **35**, 320–321, May, 1956.

Benevenutus Grassus, the most renowned European ophthalmologist of the Middle Ages, wrote a textbook of ophthalmology which remained the standard for 500 years, and became the first such work to be printed (in 1474, the year before its metaphysical rival, the *Liber de Oculo Morali* of John of Peckham, later Archbishop of Canterbury). That he was far in advance of his time is perhaps evidenced by one of his salves for external eye affections, which consisted of zinc oxide mixed with wine. *P. D. Trevor-Roper*

1619. **The Greek *Editio princeps* of Galen (1525), Its Origin and Its Influence.** (Die griechische Editio princeps des Galenos (1525), ihre Entstehung und ihre Wirkung)
N. MANI. *Gesnerus* [*Gesnerus* (*Aarau*)] **13**, 29–52, 1956. Bibliography.

This is a scholarly study of the means by which the writings of Galen were carried over from the stage of manuscript in the later Middle Ages to that of printed works in the new age of the Renaissance.

The keystone in this bridge of transition was the Greek edition which appeared from the Aldine Press at Venice in 1525, ten years after the death of the famous publisher Aldo Manuzio. Its importance lay in the fact that it offered to the many who were to translate Galen's works into Latin a convenient and accessible text. Many Latin editions were published and, as time went on, various Greek manuscripts were discovered and included. By means of those editions, especially those from the printing houses of Guinti and of Froben, the writings of Galen were arranged systematically from the medical point of view, a distinction was made between the authentic and the dubious works, and Galen became re-established as an accessible and useful authority, whose collected works ranked with the *Canon* of Avicenna.

[Even today there is much to be learned from Galen, and this excellent exposition of the sources and of the evolution of the printed works will be welcomed by all medical bibliographers. That the author has been thorough is shown by the clearly documented footnotes, 103 in number. There is also an interesting full-page diagram, illustrating the genealogy of the Galen tradition during the period under review.]
Douglas Guthrie

1620. **An Early Victorian Surgeon–Cardiologist (James Wardrop, 1782–1869)**
P. T. O'FARRELL. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 271–275, No. 366, June, 1956. 3 refs.

1621. **Sir Kenelm Digby on Folie à deux. An Historical Note**
H. P. GREENBERG, R. A. HUNTER, and I. MACALPINE. *British Journal of Medical Psychology* [*Brit. J. med. Psychol.*] **29**, 294–297, 1956 (Parts 3 and 4). 33 refs.

1622. **Two Types of Respiratory Apparatus of Stephen Hales**
R. FOREGGER. *Anaesthesia* [*Anaesthesia*] **11**, 235–240, July, 1956. 2 figs., 8 refs.

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